
From: Jorgenson, Lyric (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=JORGENSENLA]
Sent: 6/21/2017 6:31:32 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Berkley, Dale (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=BERKLEYD]; Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]
Subject: link in KEI response

This link doesn't work

<https://www.broadinstitute.org/partnerships/office-strategic-alliances-and-partnering/information-about-licensing-crispr-genome-ed>

Lyric Jorgenson, PhD
Deputy Director, Office of Science Policy
National Institutes of Health
jorgensonla@od.nih.gov
301.496.6837



From: Petrik, Amy (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=C4EC05A179F04067B61F20605E911E7C-PETRIKA]
Sent: 12/13/2017 7:49:41 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]
CC: Salata, Carol (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f98ca6a1f9fc4cfdbbf4036ca8cbace4-csalata]; Feliccia, Vincent (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7f3a54860cb941c1abe1df786e478e00-vfeliccia]
Subject: RE: Final Determination for A-419-2017 for review

Thanks, Mark.

b5

I'll appreciate any advice.
Thanks,
Amy

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, December 13, 2017 2:43 PM
To: Petrik, Amy (NIH/NIAID) [E] <amy.petrik@nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Cc: Salata, Carol (NIH/NIAID) [E] <csalata@niaid.nih.gov>; Feliccia, Vincent (NIH/NIAID) [E] <vfeliccia@niaid.nih.gov>
Subject: RE: Final Determination for A-419-2017 for review

Thanks Amy,

b5

b5

From: Petrik, Amy (NIH/NIAID) [E]
Sent: Wednesday, December 13, 2017 2:30 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Cc: Salata, Carol (NIH/NIAID) [E] <csalata@niaid.nih.gov>; Feliccia, Vincent (NIH/NIAID) [E] <vfeliccia@niaid.nih.gov>
Subject: Final Determination for A-419-2017 for review

Hi Mark and Dale,

I've drafted the attached final determination for the proposed PaxVax exclusive license to the NIAID Zika vaccine technology, with input from my TTIPO colleagues.

Would you each, please, review and let me know if you have any suggestions/edits to improve it?

If you have any questions, please don't hesitate to call.
Thanks,
Amy

Amy F. Petrik, Ph.D.
Technology Transfer and Patent Specialist

REL0000024281

Technology Transfer and Intellectual Property Office
National Institute of Allergy and Infectious Diseases
National Institutes of Health, HHS

5601 Fishers Lane
Suite 2G
Rockville, MD 20892-9804
240-627-3721

March-In Rights Under the Bayh-Dole Act

John R. Thomas
Visiting Scholar

September 23, 2016

Congressional Research Service

7-5700

www.crs.gov

R44640

Summary

Congress approved the Bayh-Dole Act, P.L. 96-517, in order to address concerns about the commercialization of technology developed with public funds. This 1980 legislation awards title to inventions made with federal government support if the contractor consists of a small business, a university, or other non-profit institution. A subsequent presidential memorandum extended this policy to all federal government contractors. As a result, the contractor may obtain a patent on its invention, providing it an exclusive right in the invention during the patent's term. The Bayh-Dole Act endeavors to use patent ownership as an incentive for private sector development and commercialization of federally funded research and development (R&D).

The federal government retains certain rights in inventions produced with its financial assistance under the Bayh-Dole Act. The government retains a "nonexclusive, nontransferable, irrevocable, paid-up license" for its own benefit. The Bayh-Dole Act also provides federal agencies with "march-in rights," codified at 35 U.S.C. §203. March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a "nonexclusive, partially exclusive, or exclusive license" to a "responsible applicant or applicants." If the patent owner refuses to do so, the government may grant the license itself.

No federal agency has ever exercised its power to march in and license patent rights to others. In particular, the National Institutes of Health (NIH) has received six march-in petitions and has denied each one. A 2016 exchange of correspondence between Members of Congress and the Department of Health and Human Services suggests a difference of views related to agency authority under the march-in provision. Supporters of the use of march-in rights assert that they provide an unused mechanism for combatting high drug prices and ensuring that U.S. citizens enjoy the benefits of public R&D funding. Others assert that march-in rights do not provide such a broad authority, but rather are limited to four circumstances identified in the statute. They are also concerned that use of march-in rights might discourage private investment in the often considerable effort needed to bring early-stage technologies to the marketplace.

Congress possesses a number of options with respect to march-in rights. If the current situation is deemed acceptable, then no action need be taken. Congress could also consider amending the Bayh-Dole Act by specifying in greater detail the precise circumstances in which march-in rights should be exercised. Congress may also take such steps as transferring authority over the administration of march-in rights, requiring government contractors to submit periodic reports regarding the commercialization of inventions achieved through public funding, creating a centralized database of inventions subject to the Bayh-Dole Act, and taking steps to ensure that patents on inventions developed through government funding are licensed to the most capable enterprise.

Contents

Introduction	1
The Patent System: An Overview.....	2
The Mechanics of the Patent System	2
Patents and Innovation Policy	3
The Bayh-Dole Act.....	5
March-In Rights	7
The Mechanics of March-In Rights	7
March-In Petitions.....	8
Debate over March-In Rights.....	10
Congressional Issues and Options	12
Concluding Observations	13

Contacts

Author Contact Information	14
----------------------------------	----

Introduction

Congressional interest in facilitating U.S. technological innovation led to the passage of P.L. 96-517, Amendments to the Patent and Trademark Act.¹ This legislation is commonly referred to as the “Bayh-Dole Act,”² after its two primary sponsors, former Senators Robert Dole and Birch Bayh. This 1980 legislation awards title to inventions that government contractors make with federal government support, if the contractor consists of a small business, a university, or other non-profit institution. A subsequent presidential memorandum extended this policy to all federal government contractors.³ As a result, the contractor may obtain a patent on its invention, providing it with an exclusive right in the invention during the patent’s term. The legislation is intended to use patent ownership as an incentive for private sector development and commercialization of federally funded research and development (R&D).

The federal government retains certain rights in inventions produced with its financial assistance under the Bayh-Dole Act. The government retains a “nonexclusive, nontransferable, irrevocable, paid-up license” for its own benefit.⁴ The Bayh-Dole Act also provides federal agencies with “march-in rights.”⁵ March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a “nonexclusive, partially exclusive, or exclusive license” to a “responsible applicant or applicants.” If the patent owner refuses to do so, the government may grant the license itself.

Members of Congress have recently taken note of the fact that march-in rights have never been exercised during the 35-year history of the Bayh-Dole Act.⁶ In particular, the National Institutes of Health (NIH) has received six march-in petitions and has denied each one. A 2016 exchange of correspondence between some Members of Congress and the Department of Health and Human Services has suggested a potential difference of views about the appropriate use of march-in rights.⁷ Some observers believe that march-in rights should be rarely, if ever invoked due to the significant investment the private sector investment may make to bring early-stage inventions into practical application. These commentators further assert that the use of march-in rights would discourage private enterprise from investing in the commercial development of any invention funded in part by the government.⁸ On the other hand, others believe that U.S. taxpayers should be protected from what they view as excessive profiteering on technologies developed with

¹ 94 Stat. 3015 (1980). For further information about this legislation, see CRS Report RL32076, *The Bayh-Dole Act: Selected Issues in Patent Policy and the Commercialization of Technology*, by Wendy H. Schacht.

² See, e.g., Fred Reinharta and Stephen J. Susalkaa, “Inspired Bayh-Dole Act Turns 35,” *les Nouvelles*, vol. 51 (March 2016), p. 17.

³ See Memorandum on Government Patent Policy from President Ronald Reagan, to Heads of Executive Departments and Agencies, February 18, 1983, <http://www.presidency.ucsb.edu/ws/index.php?pid=40945&st=&st1=>.

⁴ 35 U.S.C. §202(c)(4).

⁵ 35 U.S.C. §203.

⁶ See, e.g., William O'Brien, “March-In Rights Under the Bayh-Dole Act: The NIH’s Paper Tiger?,” *Seton Hall Law Review*, vol. 43 (2013), p. 1403.

⁷ See Michael Mezher, “Lawmakers Urge HHS to Exercise ‘March-In’ Rights to Fight Higher Drug Costs,” *States News Service*, January 11, 2016.

⁸ Letter from Patricia Harsche Weeks, Immediate Past President, Association of University Technology Managers, to Dr. Mark Rohrbaugh, Director of the Office of Technology Transfer, NIH; <http://www.autm.net/advocacy-topics/government-issues/advocacy-archives/march-in-rights/autm-response-to-march-in-provisions/>.

public funding. They consider march-in rights to constitute a long-available, but entirely unused mechanism for combatting the high and growing cost of health care.⁹

This report reviews the availability of march-in rights under the Bayh-Dole Act. It begins by providing a brief overview of the patent system and innovation policy. The report then introduces the Bayh-Dole Act. The specific details of the march-in authority provided to federal agencies are reviewed next. The report then considers past efforts to obtain march-in authorization from NIH. The report closes with an identification of potential issues for congressional consideration.

The Patent System: An Overview

The Mechanics of the Patent System

The patent system is grounded in Article I, Section 8, Clause 8 of the U.S. Constitution, which states that “The Congress Shall Have Power ... To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries....” As mandated by the Patent Act of 1952,¹⁰ U.S. patent rights do not arise automatically. Inventors must prepare and submit applications to the U.S. Patent and Trademark Office (USPTO) if they wish to obtain patent protection.¹¹ USPTO officials known as examiners then assess whether the application merits the award of a patent.¹² The patent acquisition process is commonly known as “prosecution.”

In deciding whether to approve a patent application, a USPTO examiner will consider whether the submitted application fully discloses and distinctly claims the invention.¹³ The examiner will also determine whether the invention itself fulfills certain substantive standards set by the patent statute. To be patentable, an invention must be useful, novel, and nonobvious. The requirement of usefulness, or utility, is satisfied if the invention is operable and provides a tangible benefit.¹⁴ To be judged novel, the invention must not be fully anticipated by a prior patent, publication or other state-of-the-art knowledge that is collectively termed the “prior art.”¹⁵ A nonobvious invention must not have been readily within the ordinary skills of a competent artisan at the time the invention was made.¹⁶

If the USPTO allows the patent to issue, the patent proprietor obtains the right to exclude others from making, using, selling, offering to sell, or importing into the United States the patented invention.¹⁷ Those who engage in these acts without the permission of the patentee during the term of the patent can be held liable for infringement. Adjudicated infringers may be enjoined from further infringing acts.¹⁸ The patent statute also provides for the award of damages

⁹ Amy R. Schfield, “The Demise of Bayh-Dole Protections Against the Pharmaceutical Industry’s Abuses of Government-Funded Inventions,” *Journal of Law, Medicine & Ethics*, vol. 32 (2004), p. 780.

¹⁰ P.L. 82-593, 66 Stat. 792 (codified at Title 35 United States Code).

¹¹ 35 U.S.C. §111.

¹² 35 U.S.C. §131.

¹³ 35 U.S.C. §112.

¹⁴ 35 U.S.C. §101.

¹⁵ 35 U.S.C. §102.

¹⁶ 35 U.S.C. §103.

¹⁷ 35 U.S.C. §271(a).

¹⁸ 35 U.S.C. §283.

“adequate to compensate for the infringement, but in no event less than a reasonable royalty for the use made of the invention by the infringer.”¹⁹

The maximum term of patent protection is ordinarily set at 20 years from the date the application is filed.²⁰ At the end of that period, others may employ that invention without regard to the expired patent.

Patent rights are not self-enforcing. Patentees who wish to compel others to observe their rights must commence enforcement proceedings, which most commonly consist of litigation in the federal courts. Although issued patents enjoy a presumption of validity, accused infringers may assert that a patent is invalid or unenforceable on a number of grounds.²¹ The U.S. Court of Appeals for the Federal Circuit (Federal Circuit) possesses national jurisdiction over most patent appeals from the district courts.²² The U.S. Supreme Court enjoys discretionary authority to review cases decided by the Federal Circuit.²³

Patents and Innovation Policy

The patent system is intended to promote innovation, which in turn leads to industry advancement and economic growth. The patent system in particular attempts to address “public goods problems” that may discourage individuals from innovating. Innovation commonly results in information that may be deemed a “public good,” in that it is both non-rivalrous and non-excludable. Stated differently, consumption of a public good by one individual does not limit the amount of the good available for use by others; and no one can be prevented from using that good.²⁴

The lack of excludability in particular is believed to result in an environment where too little innovation would occur. Absent a patent system, “free riders” could easily duplicate and exploit the inventions of others. Further, because they incurred no cost to develop and perfect the technology involved, copyists could undersell the original inventor. Aware that they would be unable to capitalize upon their inventions, individuals might be discouraged from innovating in the first instance. The patent system corrects this market failure problem by providing innovators with an exclusive interest in their inventions, thereby allowing them to capture their marketplace value.²⁵

The patent system potentially serves other goals as well. The patent law may promote the disclosure of new products and processes, as each issued patent must include a description sufficient to enable skilled artisans to practice the patented invention.²⁶ In this manner the patent

¹⁹ 35 U.S.C. §284.

²⁰ 35 U.S.C. §154(a)(2). Although patent term is based upon the filing date, the patentee gains no enforceable legal rights until the USPTO allows the application to issue as a granted patent. A number of Patent Act provisions may modify the basic 20-year term, including examination delays at the USPTO and delays in obtaining marketing approval for the patented invention from other federal agencies.

²¹ 35 U.S.C. §282.

²² 28 U.S.C. §1295(a)(1).

²³ 28 U.S.C. §1254(1).

²⁴ See Deepa Varadarajan, “Of Fences and Definite Patent Boundaries,” *Vanderbilt Journal of Entertainment and Technology Law*, vol. 18 (Spring 2016), p. 563.

²⁵ See Gregory N. Mandel, “Innovation Rewards: Solving the Twin Market Failures of Public Goods,” *Vanderbilt Journal of Entertainment and Technology Law*, vol. 18 (Winter 2016), p. 303.

²⁶ 35 U.S.C. §112.

system ultimately contributes to the growth of information in the public domain. Issued patents may encourage others to “invent around” the patentee’s proprietary interest. A patent proprietor may point the way to new products, markets, economies of production, and even entire industries. Others can build upon the disclosure of a patent instrument to produce their own technologies that fall outside the exclusive rights associated with the patent.²⁷

The patent system also has been identified as a facilitator of markets. If inventors lack patent rights, they may have scant tangible assets to sell or license. In addition, an inventor might otherwise be unable to police the conduct of a contracting party. Any technology or know-how that has been disclosed to a prospective licensee might be appropriated without compensation to the inventor. The availability of patent protection decreases the ability of contracting parties to engage in opportunistic behavior. By lowering such transaction costs, the patent system may make transactions concerning information goods more feasible.²⁸

Patent protection may also encourage enterprises to commercialize and market existing inventions. Even though a new technology has already been patented, a firm might have to make refinements, construct manufacturing facilities, establish distribution channels, comply with government safety and regulatory requirements, and educate consumers prior to marketing. Second entrants to the market may not have to bear all of the first mover’s costs. As a result, the exclusive rights provided by a patent may encourage not just the invention of new technologies, but also their commercialization.²⁹

Through these mechanisms, the patent system may act in a more socially desirable way than its chief legal alternative, trade secret protection.³⁰ Trade secrecy guards against the improper appropriation of valuable, commercially useful, and secret information.³¹ In contrast to patenting, trade secret protection does not result in the disclosure of publicly available information. That is because an enterprise must take reasonable measures to keep secret the information for which trade secret protection is sought. Taking the steps necessary to maintain secrecy, such as implementing physical security measures, also imposes costs that may ultimately be unproductive for society.

The patent system has long been subject to criticism, however. Some observers have asserted that the patent system is unnecessary due to market forces that already suffice to create an optimal level of innovation. The desire to obtain a lead time advantage over competitors may itself provide sufficient inducement to invent without the need for further incentives. Other commentators believe that the patent system encourages industry concentration and presents a barrier to entry in some markets. Additionally, while the patent incentive encourages the development of new medicines, some assert that it also contributes to the growing costs of healthcare.³²

²⁷ See Herbert Hovenkamp, “Antitrust and the Patent System: A Reexamination,” *Ohio State Law Journal*, vol. 76 (2015), p. 467.

²⁸ Jonathan N. Barnett, “Cultivating the Genetic Commons: Imperfect Patent Protection and the Network Model of Innovation,” *San Diego Law Review*, vol. 36 (2000), p. 1029-1030.

²⁹ Emily Michiko Morris, “The Many Faces of Bayh-Dole,” *Duquesne Law Review*, vol. 54, p. 81.

³⁰ For further information on trade secrets, see CRS Report R43714, *Protection of Trade Secrets: Overview of Current Law and Legislation*, by Brian T. Yeh.

³¹ See generally Michael R. McGurk and Jia W. Lu, “The Intersection of Patents and Trade Secrets,” *Hastings Science & Technology Law Journal*, vol. 7 (Summer 2015), p. 189.

³² See, e.g., Dan L. Burk and Mark A. Lemley, *The Patent Crisis and How the Courts Can Solve It* (2009); James Bessen and Michael Meurer, *Patent Failure: How Judges, Bureaucrats, and Lawyers Put Innovators at Risk* (2008); (continued...)

Each of these arguments for and against the patent system has some measure of intuitive appeal. However, they remain difficult to analyze on an empirical level. We lack rigorous analytical methods for studying the impact of the patent system upon the economy as a whole. As a result, current economic and policy tools do not allow us to calibrate the patent system precisely in order to produce an optimal level of investment in innovation at the lowest social costs.

The Bayh-Dole Act

Even prior to the Bayh-Dole Act, the federal government considered the intellectual property implications of R&D projects financed by public funds.³³ In 1963, the Kennedy Administration called for greater consistency in diverse agency practices regarding the disposition of rights to inventions made by government contractors. This early “Government Patent Policy” generally allowed the U.S. government to retain rights to inventions developed through government contracts.³⁴ However, the contractor could obtain title in specified circumstances. For example:

[W]here the purpose of the contract is to build upon existing knowledge or technology to develop information, products, processes, or methods for use by the government, and the work called for by the contract is in a field of technology in which the contractor has acquired technical competence (demonstrated by factors such as know-how, experience, and patent position) directly related to an area in which the contractor has an established nongovernmental commercial position, the contractor shall normally acquire the principal or exclusive rights throughout the world in and to any resulting inventions, subject to the government acquiring at least an irrevocable non-exclusive royalty free license throughout the world for governmental purposes.³⁵

In those situations, the 1963 policy retained significant government rights in privately held patents that resulted from publicly funded projects. In a prelude to today’s march-in rights, the 1963 policy further provided:

Where the principal or exclusive (except as against the government) rights to an invention are acquired by the contractor, the government shall have the right to require the granting of a license to an applicant royalty free or on terms that are reasonable in the circumstances to the extent that the invention is required for public use by governmental regulations or as may be necessary to fulfill health needs, or for other public purposes stipulated in the contract.³⁶

The 1980 enactment of the Bayh-Dole Act altered the intellectual property landscape with respect to patents and government-sponsored R&D. Congress instead accepted the proposition that the lack of patent title discouraged private enterprise from advancing early-stage technologies into the marketplace. For example, suppose that a university researcher identifies a promising chemical compound using funds provided by the National Institutes of Health (NIH). Some observers believed that under pre-Bayh-Dole Act practices, a brand-name pharmaceutical company would be unlikely to undertake costly and risky clinical trials in order to convert that

(...continued)

Adam B. Jaffe and Josh Lerner, *Innovation and Its Discontents: How Our Broken Patent System Is Endangering Innovation and Progress, and What To Do About It* (2004).

³³ Roberto Mazzoleni, “Patents and University-Industry Interactions in Pharmaceutical Research Before 1962: An Investigation of the Historical Justifications for Bayh-Dole,” *Journal of High Technology Law*, vol. 10 (2010), p. 168.

³⁴ “Statement of Government Patent Policy,” 28 *Federal Register* 10943, October 10, 1963.

³⁵ *Ibid.* at 10945.

³⁶ *Ibid.*

early-stage research into a drug approved by the Food and Drug Administration. Absent patent protection, generic firms could quickly introduce competing products. This view accepts that patents provide incentives not just for individuals to invent, but also to commercialize completed inventions.³⁷

Under the Bayh-Dole Act, each nonprofit organization (including universities) or small business is permitted to elect within a reasonable time to retain title to any “subject invention” made under federally funded R&D.³⁸ The institution must commit to commercialization of the invention within a predetermined, agreed upon, timeframe. However, the government may keep title under “exceptional circumstances when it is determined by the agency that restriction or elimination of the right to retain title to any subject invention will better promote the policy and objectives of this chapter.” Additionally, the government may withhold title if the contractor “is not located in the United States or does not have a place of business located in the United States or is subject to the control of a foreign government”; in situations associated with national security; or when the work is related to the naval nuclear propulsion or weapons programs of the Department of Energy.³⁹

Certain other rights are reserved for the government. The government retains “a nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States any subject invention throughout the world....”⁴⁰ The government also retains “march-in rights” which enable the federal agency to require the contractor to license a third party to use the invention under certain circumstances.⁴¹ This report discusses march-in rights at greater length below.

By its own terms, the Bayh-Dole Act applies only to nonprofit organizations (including universities) and small businesses. However, in a February 1983 memorandum concerning the vesting of title to inventions made under federal funding, then-President Ronald Reagan ordered all agencies to treat, as allowable by law, all contractors within the Bayh-Dole Act framework regardless of their size.⁴² This longstanding practice lacks a legislative basis, however.

The Bayh-Dole Act authorizes the government to withhold public disclosure of information for a “reasonable time” until a patent application can be made.⁴³ Licensing by any contractor retaining title under this act is restricted to companies that will manufacture substantially within the United States. This requirement may be waived if domestic manufacture is not commercially feasible, or if the contractor or its successors made reasonable but ultimately unsuccessful efforts to license domestic manufacturers.⁴⁴ The Secretary of Commerce was provided the authority to issue regulations implementing the Bayh-Dole Act.⁴⁵

³⁷ See F. Scott Kieff, “Property Rights and Property Rules for Commercializing Inventions,” *Minnesota Law Review*, vol. 85 (2001), p. 697.

³⁸ 35 U.S.C. §202(a).

³⁹ *Ibid.*

⁴⁰ 35 U.S.C. §202(c)(4).

⁴¹ 35 U.S.C. §203.

⁴² Memorandum on Government Patent Policy from President Ronald Reagan, to Heads of Executive Departments and Agencies, February 18, 1983, <http://www.presidency.ucsb.edu/ws/index.php?pid=40945&st=&st1=>.

⁴³ 35 U.S.C. §205.

⁴⁴ 35 U.S.C. §204.

⁴⁵ 35 U.S.C. §206. These regulations may be found at 37 C.F.R. Part 401.

March-In Rights

The Mechanics of March-In Rights

The Bayh-Dole Act provides the government with the ability to “march in” and grant licenses for patents that resulted from publicly funded R&D. In particular, march-in rights allow the federal government, in specified circumstances, to require the contractor or successors in title to the patent to grant a “nonexclusive, partially exclusive, or exclusive license” to a “responsible applicant or applicants.”⁴⁶ If the patent owner refuses to do so, the government may grant the license itself. The terms of the license must be “reasonable under the circumstances.”

The Bayh-Dole Act specifies four circumstances under which march-in rights may be exercised. The federal agency that provided the funding arrangement under which the patented invention was made must reach one of the following determinations:

- (1) action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use;
- (2) action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees;
- (3) action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees; or
- (4) action is necessary because the agreement required by section 204 [generally requiring that patented products be manufactured substantially in the United States unless domestic manufacture is not commercially feasible] has not been obtained or waived or because a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of its agreement obtained pursuant to section 204.⁴⁷

With respect to the first of these conditions, the Bayh-Dole Act further defines the term “practical application” as “to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms.”⁴⁸

The Bayh-Dole Act states that any adversely affected “contractor, inventor, assignee, or exclusive licensee” may appeal a march-in rights petition to the United States Court of Federal Claims. The statute further explains that in cases described in paragraphs (1) and (3) above, march-in authority may not actually be exercised until all appeals or petitions are exhausted.⁴⁹

The exercise of march-in rights does not invalidate or void the relevant patent. That patent remains extant and could presumably be enforced against entities that did not enjoy march-in rights. However, march-in rights grant a license—in other words, a permission—to the enterprise identified by the government. That entity may practice the patented invention without concern for

⁴⁶ 35 U.S.C. §203(a).

⁴⁷ 35 U.S.C. §203(a).

⁴⁸ 35 U.S.C. §201(f).

⁴⁹ 35 U.S.C. §203(b).

infringement, so long as it satisfies the conditions stipulated in the march-in order, such as the payment of a royalty.

March-in rights should be distinguished from the “nonexclusive, nontransferable, irrevocable, paid-up license” that the Bayh-Dole Act grants the U.S. government elsewhere.⁵⁰ This license solely benefits the federal government. Should another entity—such as a generic drug company or other enterprise—wish to practice the patented invention, then march-in rights provide a possible legal mechanism.

March-in rights are also distinct from the workings of another statute, 28 U.S.C. §1498(a).⁵¹ That provision states:

Whenever an invention described in and covered by a patent of the United States is used or manufactured by or for the United States without license of the owner thereof or lawful right to use or manufacture the same, the owner’s remedy shall be by action against the United States in the United States Court of Federal Claims for the recovery of his reasonable and entire compensation for such use and manufacture.

28 U.S.C. §1498(a) operates independently of the Bayh-Dole system. That statute applies to the use of a patented invention by the U.S. government, or one of its contractors with the authorization or consent of the U.S. government, without the permission of the patent proprietor. In such a case, the sole remedy for the patent owner is a suit in the U.S. Court of Federal Claims for monetary damages. An injunction is not available to the patent owner in such cases.

Three significant distinctions exist between march-in rights under the Bayh-Dole Act and 28 U.S.C. §1498(a). First, march-in rights apply only to patented inventions that were developed with the support of public funding. 28 U.S.C. §1498(a) applies to every U.S. patent, no matter what the sources of funding were. Second, private enterprises may take the initiative in requesting march-in rights from the government. 28 U.S.C. §1498(a) applies when the federal government practices the patented invention on its own behalf or requests a contractor to do so. Finally, recipients of march-in rights are awarded licenses “upon terms that are reasonable under the circumstances” and would presumably pay royalties to the patent proprietor. In contrast, under 28 U.S.C. §1498(a) the patent proprietor commences litigation and may be awarded damages to compensate for the use of the government or its contractors.

March-In Petitions

March-in rights have never been exercised during the 35-year history of the Bayh-Dole Act. Apparently the only federal agency that has even received a petition is the National Institutes of Health (NIH).⁵² In particular, six petitions have been filed requesting that the NIH “march in” with respect to a particular pharmaceutical. Each petition was denied. A common theme of each

⁵⁰ 35 U.S.C. §202(c)(4).

⁵¹ See Justin Torres, “The Government Giveth, and the Government Taketh Away: Patents, Takings, and 28 U.S.C. § 1498,” *New York University Annual Survey of American Law*, vol. 63 (2007), p. 315; Bradley M. Taub, “Why Bother Calling Patents Property? The Government’s Path to License Any Patent and Maybe Pay For It,” *John Marshall Review of Intellectual Property Law*, vol. 6, p. 151.

⁵² The author of this report has not located any record of any march-in petition filed at any other federal agency that funds R&D. See U.S. Government Accountability Office, *Federal Research: Information on the Government’s Right to Assert Ownership Control Over Federally Funded Inventions*, GAO-09-742, July 2009, <http://www.gao.gov/assets/300/293020.pdf> (noting that the Department of Defense, Department of Energy, and National Aeronautics and Space Administration “have neither discovered nor received information that would lead them to initiate a march-in proceeding or exercise their march-in authority during the last 20 years.”).

of the denials was the agency's views that concerns over drug pricing were not, by themselves, sufficient to provoke march-in rights. The six requests were:

CellPro, Inc. (1997). CellPro requested that the government exercise march-in rights after being found to infringe patents held by the contractor. Although the NIH recognized that CellPro's device was the only FDA-approved product on the market, the agency observed that (1) the contractor and its licensees had not sought immediately to enjoin CellPro and (2) that they were making reasonable efforts to commercialize their own product. As a result, the agency declined to initiate march-in procedures.⁵³

Norvir/ritonavir (2004). The petitioners, which included some Members of Congress, asked the NIH to exercise march-in rights due to perceived concerns over the high price of this HIV/AIDS treatment. The agency declined to initiate march-in proceedings because it deemed Abbott Laboratories, Inc., to have made the drug available to the public on a sufficient basis.⁵⁴

Xalatan/latanoprost (2004). Petitioners asserted that the price of this glaucoma treatment was higher than that of other nations. The NIH declined to initiate march-in proceedings because the drug was readily available for use by the public.⁵⁵

Fabrazyme/agalsidase beta (2010). This petition asked the NIH to grant an open license on certain patents relating to this treatment for Fabry disease. According to the petitioners, Genzyme Corporation was encountering difficulties in manufacturing sufficient quantities of the drug. The NIH did not initiate a march-in proceeding because (1) Genzyme was working diligently to resolve its manufacturing difficulties and (2) other enterprises were unlikely to obtain FDA marketing approval on agalsidase beta products before those problems were addressed.⁵⁶

Norvir/ritonavir (2012). The second petition against this HIV/AIDS drug more specifically requested the NIH to invoke march-in rights when prices in the United States were greater than other high-income nations. The NIH did not initiate march-in right proceedings because, in the view of the agency, such pricing disparities did not trigger any of the four statutory criteria for marching in.⁵⁷

Xtandi/enzalutamide (2016). The petitioner asserted both that the prostate cancer drug Xtandi had an average wholesale price of \$129,269 per year; and that this price was much higher than in other high-income nations. The NIH declined to

⁵³ Harold Varmus, Director, NIH, *Determination in the Case of Petition of CellPro, Inc.*, August 1, 1997, http://web.archive.org/web/20070102183356/http://www.nih.gov/icd/od/foia/cellpro/pdfs/foia_cellpro39.pdf.

⁵⁴ Elias A. Zerhouni, Director, NIH, *In the Case of Norvir Manufactured by Abbott Laboratories, Inc.*, July 29, 2004, <http://www.ott.nih.gov/sites/default/files/documents/policy/March-In-Norvir.pdf>.

⁵⁵ Elias A. Zerhouni, Director, NIH, *In the case of Xalatan, Manufactured by Pfizer, Inc.*, September 17, 2004, <https://www.ott.nih.gov/sites/default/files/documents/policy/March-in-xalatan.pdf>.

⁵⁶ Francis S. Collins, Director, NIH, *Determination in the Case of Fabrazyme Manufactured by Genzyme Corporation*, December 1, 2010, <https://www.ott.nih.gov/sites/default/files/documents/policy/March-In-Fabrazyme.pdf>.

⁵⁷ Francis S. Collins, Director, NIH, *Determination in the Case of Norvir Manufactured by AbbVie*, November 1, 2013, <https://www.ott.nih.gov/sites/default/files/documents/policy/March-In-Norvir2013.pdf>.

initiate a march-in investigation because sales of the product were increasing and no evidence suggested that the product was in short supply.⁵⁸

The NIH has offered some observations about the role of march-in rights during these proceedings. In its response to the 1997 CellPro petition, the agency stated its reluctance to undermine the exclusivities offered by the patent system:

We are wary, however, of forced attempts to influence the marketplace for the benefit of a single company, particularly when such actions may have far-reaching repercussions on many companies' and investors' future willingness to invest in federally funded medical technologies. The patent system, with its resultant predictability for investment and commercial development, is the means chosen by Congress for ensuring the development and dissemination of new and useful technologies. It has proven to be an effective means for the development of health care technologies. In exercising its authorities under the Bayh-Dole Act, NIH is mindful of the broader public health implications of a march-in proceeding, including the potential loss of new health care products yet to be developed from federally funded research.⁵⁹

In the 2004 proceedings regarding Norvir/ritonavir, the agency spoke more specifically about drug pricing:

Finally, the issue of the cost or pricing of drugs that include inventive technologies made using Federal funds is one which has attracted the attention of Congress in several contexts that are much broader than the one at hand. In addition, because the market dynamics for all products developed pursuant to licensing rights under the Bayh-Dole Act could be altered if prices on such products were directed in any way by NIH, the NIH agrees with the public testimony that suggested that the extraordinary remedy of march-in is not an appropriate means of controlling prices. The issue of drug pricing has global implications and, thus, is appropriately left for Congress to address legislatively.⁶⁰

The NIH has also observed that another statute, the Drug Price Competition and Patent Term Restoration Act, P.L. 98-417, plays a role in the public availability of medicines.⁶¹ Better known as the Hatch-Waxman Act, this legislation allows generic drug companies to develop their own products without incurring liability for patent infringement. It also allows generic drug companies to market their products prior to the expiration of relevant patents, although if they do so they may incur infringement liability at that time.⁶²

Debate over March-In Rights

Concerns over the lack of assertion of march-in rights have been expressed for the past two decades. In 2001, Peter S. Arno⁶³ and Michael H. Davis⁶⁴ published an article in the *Tulane Law*

⁵⁸ Letter from Francis C. Collins, Director, NIH, to Andrew S. Goldman, Knowledge Ecology International, June 20, 2016, <http://keionline.org/sites/default/files/Final-Response-Goldman-6.20.2016.pdf>.

⁵⁹ Harold Varmus, Director, NIH, *Determination in the Case of Petition of CellPro, Inc.*, August 1, 1997, http://web.archive.org/web/20070102183356/http://www.nih.gov/icd/od/foia/cellpro/pdfs/foia_cellpro39.pdf.

⁶⁰ Elias A. Zerhouni, Director, NIH, *In the Case of Norvir Manufactured by Abbott Laboratories, Inc.*, July 29, 2004, <http://www.ott.nih.gov/sites/default/files/documents/policy/March-In-Norvir.pdf>.

⁶¹ Francis S. Collins, Director, NIH, *Determination in the Case of Fabrazyme Manufactured by Genzyme Corporation*, December 1, 2010, <https://www.ott.nih.gov/sites/default/files/documents/policy/March-In-Fabrazyme.pdf>, p. 9.

⁶² CRS Report R41114, *The Hatch-Waxman Act: Over a Quarter Century Later*, by Wendy H. Schacht and John R. Thomas, *The Hatch-Waxman Act: Over a Quarter Century Later*.

⁶³ Dr. Arno was then a Professor of the Albert Einstein College of Medicine/Montefiore Medical Center.

⁶⁴ Mr. Davis was then a Professor of the Cleveland State College of Law.

Review asserting that the Bayh-Dole Act “has had a powerful price-control clause since its enactment in 1980 that mandates that inventions resulting from federally funded research must be sold at reasonable prices.”⁶⁵ According to Arno and Davis, “the solution to high drug prices does not involve new legislation but already exists in the unused, unenforced march-in provision of the Bayh-Dole Act.”⁶⁶ Arno and Davis followed this article with a 2002 editorial published in the *Washington Post*, stating in part:

Although Bayh-Dole has been in place for 20 years, the government has never enforced it—not even once. That, despite the AIDS crisis at home and abroad, despite the millions of elderly and chronically ill Americans in need of affordable prescription drugs and the 40 million others who have no health insurance coverage whatever—and despite the general hand-wringing over the skyrocketing costs of pharmaceuticals.⁶⁷

Former Senators Birch Bayh and Robert Dole, as they were then, responded with an editorial published in the *Washington Post* less than a month later. The editorial states in part:

Bayh-Dole did not intend that government set prices on resulting products. The law makes no reference to a reasonable price that should be dictated by the government.... The [Arno and Davis] article also mischaracterizes the rights retained by the government under Bayh-Dole. The ability of the government to revoke a license granted under the act is not contingent on the pricing of the resulting product or tied to the profitability of a company that has commercialized a product that results in part from government-funded research. The law instructs the government to revoke such licenses only when the private industry collaborator has not successfully commercialized the invention as a product.⁶⁸

Dialogue over the use of march-in rights was renewed in 2016, resulting in several exchanges between some Members of Congress, on one hand, and the Department of Health and Human Services (HHS) on the other. In an undated letter that was reportedly sent on January 11, 2016, the Honorable Lloyd Doggett, joined by 51 Members of Congress, addressed a letter to Secretary Sylvia Matthews Burwell of HHS and NIH Director Francis S. Collins. The letter in part requested NIH to provide official guidance regarding the situations in which march-in rights should apply.⁶⁹

Secretary Burwell responded by letter on March 2, 2016. Her letter states in part that the Bayh-Dole Act’s march-in right was “strictly limited and can only be exercised if the agency conducts an investigation and determines that specific criteria are met, such as alleviating health or safety needs or when effective steps are not being taken to achieve practical application of the inventions.” She also concluded that “the statutory criteria are sufficiently clear and additional guidance is not needed.”⁷⁰

Representative Lloyd Doggett sent an additional letter to Secretary Burwell and Director Collins on March 28, 2016. Signed by eleven other Members of Congress, the letter encourages the NIH

⁶⁵ Peter S. Arno and Michael H. Davis, “Why Don’t We Enforce Existing Drug Price Controls? The Unrecognized and Unenforced Reasonable Pricing Requirements Imposed Upon Patents Deriving in Whole or in Part from Federally Funded Research,” 75 *Tulane Law Review* (2001), p. 631.

⁶⁶ *Ibid.*

⁶⁷ Peter Arno and Michael Davis, “Paying Twice For the Same Drugs,” *Washington Post*, March 27, 2002, at A21.

⁶⁸ See Birch Bayh and Robert Dole, “Our Law Helps Patients Get New Drugs Sooner,” *Washington Post*, April 11, 2002, at A28.

⁶⁹ Michael Mezher, “Lawmakers Urge HHS to Exercise ‘March-In’ Rights to Fight Higher Drug Costs,” *States News Service*, January 11, 2016.

⁷⁰ Letter from Sylvia M. Burwell, Secretary of Health and Human Services, to The Honorable Lloyd Doggett, U.S. House of Representatives, March 2, 2016, <http://freepdfhosting.com/be7532cfc0.pdf>.

to conduct a public hearing regarding the request of public interest groups to invoke march-in rights to the cancer drug Xtandi/enzalutamide. The letter explains:

NIH was recently petitioned to exercise these march-in rights on Xtandi, a prostate cancer drug developed at the University of California, Los Angeles (UCLA) through taxpayer supported research grants from the U.S. Army and NIH grants. The petition states that a Japanese licensee, Astellas, is charging Americans \$129,000 for this drug, which sells in Japan and Sweden for \$39,000, and in Canada for \$30,000. We do not think that charging U.S. residents more than anyone else in the world meets the obligation to make the invention available to U.S. residents on reasonable terms.⁷¹

As noted above, the NIH denied march-rights for Xtandi/enzalutamide on June 20, 2016.⁷²

Congressional Issues and Options

To date, no bills have been introduced in the 114th Congress to address march-in rights under the Bayh-Dole Act. Therefore, if Congress deems the current situation to be acceptable, then no action need be taken. Other options include clarifications that further stipulate the circumstances under which march-in rights may be invoked, either by statutory amendment or the encouragement of regulatory refinements. Congress could, for example, define with greater clarity the precise circumstances under which a patented invention is deemed “available to the public on reasonable terms.”⁷³ Congress could also define with greater specificity when march-in rights are needed to “alleviate health or safety needs,”⁷⁴ particularly with respect to inventions that might be perceived as too costly for many consumers to afford.

Other options include transfer of oversight of administering march-in rights. Currently the Bayh-Dole Act assigns the agency that provided funds that led to the patented invention responsibility for exercising these rights.⁷⁵ Another entity might have distinct perspectives than the funding agency and might reach different conclusions on whether to exercise march-in rights.

Transferring decisionmaking authority to a distinct entity might also eliminate any perceived conflicts of interest with respect to march-in rights. Former employees of federal agencies often wish to pursue careers within the private sector and may wish to maintain good relationships with those enterprises. In addition, agency officials may themselves be named inventors on patents to which march-in rights apply.⁷⁶ These factors could conceivably lead to a perception of bias against the institution of march-in rights.

Some commentators have also suggested that Congress should establish a centralized database of inventions subject to the Bayh-Dole Act.⁷⁷ Such a record would potentially improve the ability of

⁷¹ Letter from Lloyd Doggett, House of Representatives, to The Honorable Sylvia Burwell, Secretary, Department of Health and Human Services, March 28, 2016, <http://freepdfhosting.com/1c677ecdfc.pdf>.

⁷² “Feds Won’t Lower Price of Prostate-Cancer Drug,” *Seattle Times*, June 21, 2016.

⁷³ 35 U.S.C. §201(f).

⁷⁴ 35 U.S.C. §203(a)(2).

⁷⁵ 35 U.S.C. §203(a).

⁷⁶ The petition for rehearing of the Fabrazyme march-in decision asserted that NIH Director Francis Collins was named as an inventor on nineteen patents potentially subject to march-in rights. Letter from C. Allen Black, Jr., Attorney at Law, to Mark Rohrbaugh, Office of Technology Transfer, NIH, April 5, 2011, <http://patentdocs.typepad.com/files/nih-petition-for-rulemaking-and-rehearing-90.pdf>.

⁷⁷ Ryan Whalen, “The Bayh-Dole Act & Public Rights in Federally Funded Inventions: Will the Agencies Ever Go Marching In?,” *Northwestern University Law Review*, vol. 109 (2015), pp. 1111-12.

the public to track its R&D investments and observe the degree to which these investments have resulted in new products for the marketplace. If a further level of monitoring were desirable, one possibility would be to require licensees of patents subject to the Bayh-Dole Act to submit periodic reports disclosing both their efforts at introducing the patented inventions to the public and their pricing policies.

Other commentators also have urged reconsideration of the statutory requirement that in certain cases all judicial appeals be exhausted before march-in authority may actually be exercised.⁷⁸ Under current law, even though a federal agency has authorized march-in rights, they may at times not be used until the patent proprietor has taken his case as far as the Supreme Court of the United States. As Arti K. Rai⁷⁹ and Rebecca S. Eisenberg⁸⁰ assert, “the tolerance for protracted delays inherent in the current process is at odds with the time-sensitive nature of the interests reflected in the substantive standard, such as achieving practical application of the invention ‘within a reasonable time’ and ‘alleviat[ing] health or safety needs.’”⁸¹ This possibility of delay could also possibly discourage march-in petitions in the first instance.

Still other commentators have suggested that Congress should take further steps to ensure that the best candidate receives licenses for patents subject to the Bayh-Dole Act. Under current law, government contractors may choose to license their inventions to anyone. Such a system may not place these inventions in the most capable hands, either from the perspective of the contractor or of the public.⁸² Another option might be an open-bidding auction that might better ensure that patents on inventions developed through government funding are licensed to the most capable enterprise.⁸³

Concluding Observations

Current dialogue over march-in rights involves a familiar policy debate in intellectual property law. On the one hand, the patent laws are intended to promote the labors that lead to innovation. Critics of the use of march-in rights believe that diluting the patent incentive will discourage private investment and ultimately work against the aims of the Bayh-Dole Act. But others say that the patent laws are also intended to distribute the fruits of those labors to the public. This goal is most visibly achieved when patents expire and previously proprietary technologies enter the public domain. However, some observers believe that march-in rights provide an unused mechanism for discouraging excessive profiteering and providing the public an appropriate return on its R&D investments during a patent’s term. Striking a balance between these competing views regarding the commercialization of federally funded research remains a matter of congressional judgment.

⁷⁸ 35 U.S.C. §203(b).

⁷⁹ Arti K. Rai is the Elvin R. Latty Professor of Law at the Duke University School of Law.

⁸⁰ Rebecca S. Eisenberg is the Robert and Barbara Luciano Professor of Law at the University of Michigan Law School.

⁸¹ Arti K. Rai and Rebecca S. Eisenberg, “Bayh-Dole Reform and the Process of Biomedicine,” *Journal of Law and Contemporary Problems*, vol. 66 (2003), p. 311.

⁸² Peter Lee, “Transcending the Tacit Dimension: Patents, Relationships, and Organizational Integration in Technology Transfer,” *California Law Review*, vol. 100 (2012), p. 1521.

⁸³ See Whalen, *supra*.

Author Contact Information

John R. Thomas
Visiting Scholar
jrthomas@crs.loc.gov, 7-0975

From: Kassilke, Deborah (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=KASSILKE]
Sent: 1/19/2017 8:19:28 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: Question re: FOIA for OTT

Good info. If I draft a response will you be so kind to review it before I hit send?

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, January 19, 2017 3:15 PM
To: Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov>
Subject: RE: Question re: FOIA for OTT

If it is public information, I would point them to it. If it is not, they should be told they can submit a FOIA. If it is something we do not track, then you could tell them that.

b5

b5

From: Kassilke, Deborah (NIH/OD) [E]
Sent: Thursday, January 19, 2017 3:05 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: Question re: FOIA for OTT

Great – can you help educate me then on how we address non- foia questions like theirs?
The last item is the one where they request royalties paid to feds, which is a foia request that is being worked for them.

Working with the Foia office on foia responses is pretty straight forward (though rarely fun). It's these that don't come in as foias that I don't understand what is proper/correct way to address. Any education/ guidance you can give me?

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, January 19, 2017 3:02 PM
To: Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov>
Subject: RE: Question re: FOIA for OTT

b5

This is not submitted as a FOIA is it? I do not see that mentioned in the emails. With FOIA we do not need to do an analysis only product documents. FOIA applies to documents or reports you can run from a database. We do not have to do analyses under a FOIA.

b5

b5

From: Kassilke, Deborah (NIH/OD) [E]
Sent: Thursday, January 19, 2017 2:50 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: FW: Question re: FOIA for OTT

Mark —

b5

I'm going to cc you when I respond back to our FOIA office to see what info they sent last year (2015) for the crada list.

b5

Thanks- I'm trying to wrap this one up.
Deb

From: Kassilke, Deborah (NIH/OD) [E]
Sent: Thursday, January 12, 2017 4:53 PM
To: Allen, Marin (NIH/OD) [E] <AllenM1@mail.nih.gov>
Cc: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: Question re: FOIA for OTT

Hello Marin —

How did you end up dealing with FOIAs? Congratulations? Grin.

Before Susan Cornell left, she was working on some OTT related FOIA requests from KEI. We have received 3 requests from them (see the attached). Before we respond I would like to know what Susan may have sent them on previous requests. How do I find out what has been issued previously?

Mark Rohrbaugh was kind enough to speak with them on the phone today and explained that CRADAs do not require a Fed Registry Notice. I'll reference that when I respond to the request from Mr. Love.

Please advise and I appreciate your help.
Deb

Deborah Kassilke
Director, Office of Technology Transfer
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, MD 20852
E-Mail: Deborah.Kassilke@nih.gov
Phone: 301-435-5294
*Cell: **b6***

REL0000024285

From: Dodson, Sara (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DODSONSE]
Sent: 12/16/2015 9:37:28 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: Documents from last meeting with Jim Onken
Attachments: DRAFT Biomedical Research Outputs and Outcomes Table 052213.xlsx; v5WHITE PAPER Gleevec_pr MLR_SED_LSR_10282015_clean for OER.docx; FHS Data Dump_1.4 12-9-15.docx; Neurotech Data Dump_ToICs.docx; OSP_CaseStudy.pdf; Hib Background and Case Study Outline 2015-08-12.docx; OSP case study methods for OER_12092015.docx

Here you go!

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, December 16, 2015 3:54 PM
To: Dodson, Sara (NIH/OD) [E]
Subject: Documents from last meeting with Jim Onken

Sara:

Could you please send me the documents from the meeting with OER? If you already sent them, could you send them again please. I cannot locate them.

Thanks,
Mark

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Office of Science Policy
National Institutes of Health

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

CHILDHOOD VACCINES: NEARLY ELIMINATING THE THREAT OF BACTERIAL MENINGITIS

By “teaching” the immune system to defend against infection, vaccination prevents serious illness, disability, and death for dozens of infectious diseases, making it one of the most important public health achievements ever. As a leader in biomedical research, NIH has contributed to many vaccines throughout its history – one standout vaccine has nearly eliminated Haemophilus influenzae type b (Hib) infection in the U.S. Once the leading cause of bacterial meningitis in children, Hib infection can result in serious, long-term disability and death. Today, the near elimination of Hib has had profound benefits throughout the world. NIH, in concert with many other governmental, non-profit, and private organizations, played a key role in making an effective Hib vaccine a reality, resulting in thousands of lives saved.

HAEMOPHILUS INFLUENZAE TYPE B (Hib)

- Bacterial infection spread through the air and direct skin contact
- Causes fever, bacterial meningitis, pneumonia, infection of the blood, and swelling of the throat and joints
- Long-term consequences can include deafness, blindness, brain damage, and intellectual disability
- Predominately affects young children, especially infants

Also see Hib information provided by the Centers for Disease Control and Prevention (CDC):

<http://www.cdc.gov/vaccines/vpd-vac/hib/default.htm>

Hib INFECTIONS: THEN AND NOW



THEN

- Antibiotics were not always prescribed at the right time, nor were they fully effective for all children infected with Hib.
- Hib was the leading cause of bacterial meningitis and acquired intellectual disability in children.
- More than 20,000 cases of Hib were reported in the U.S. each year.
- Upwards of 1,000 children died from Hib every year and 6,000 suffered from deafness, seizures, intellectual disability, or brain damage primarily due to bacterial meningitis.
- \$2 billion per year in health care costs were attributed to Hib and related illnesses in 1968.

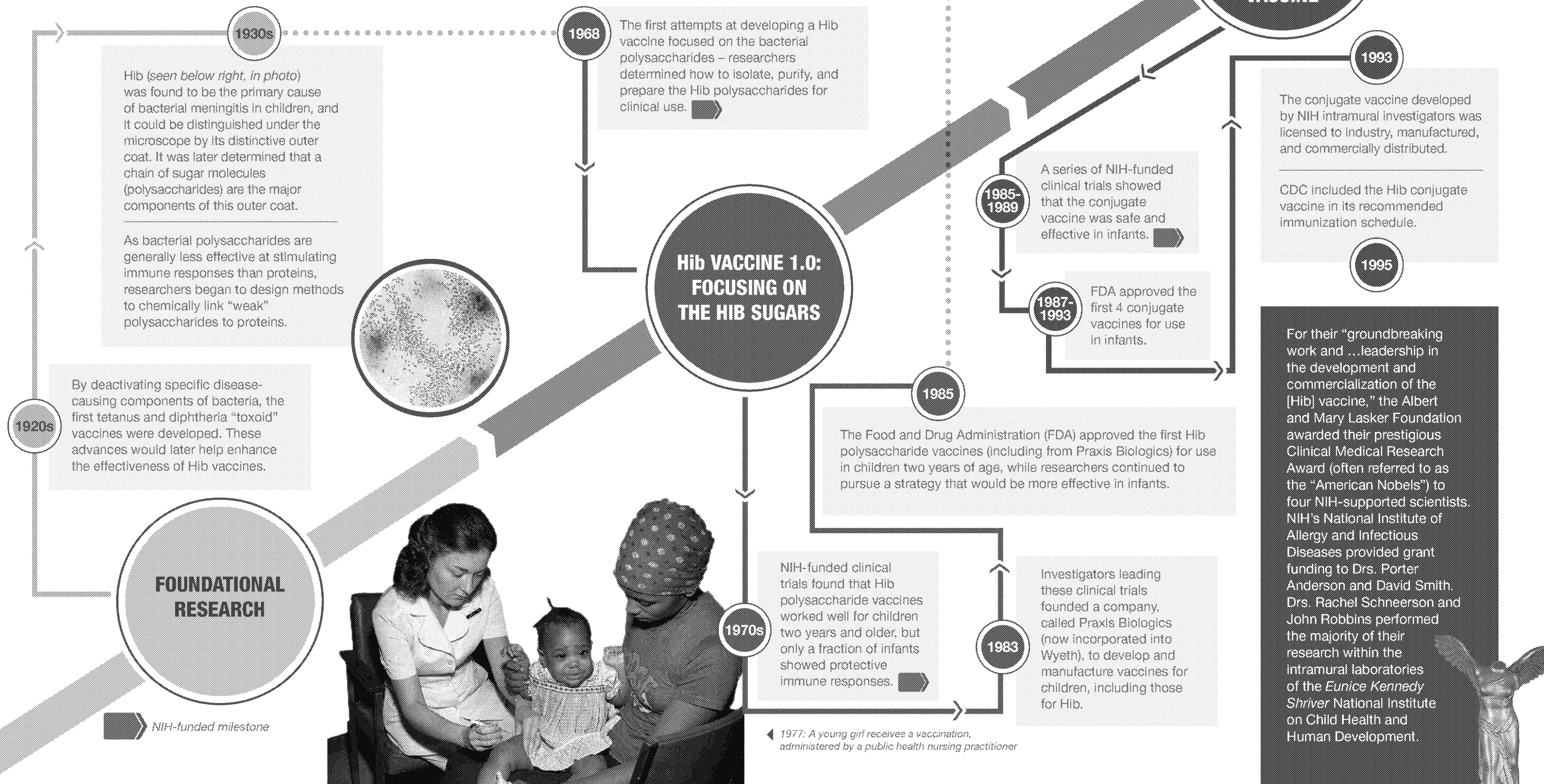


NOW

- Highly effective Hib vaccines have been in use since the late 1980s.
- More than 90% of children in the U.S. received a Hib vaccine in 2014.
- The CDC predicts that more than 19,000 cases and 700 Hib-related deaths will be prevented over the lifespan of the 4 million U.S. children born in 2009 alone.
- For the group of children born in 2009, Hib vaccination is predicted to save \$1.8 billion in direct costs and \$3.7 billion in total societal costs.

**Cases have
dropped by more
than 99%, with
only around 40
reported in 2009.**

RESEARCH-TO-PRACTICE MILESTONES FOR THE Hib VACCINE



IMPACTS OF Hib VACCINES

HEALTH

- First conjugate vaccine approved to treat an infectious disease.
- More than 90% of children in the U.S. receive the Hib vaccine.

Incidence of Hib cases declined **more than 99%** following availability of the conjugate vaccine.



SOCIETY

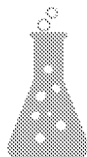
- Hospitalization for Hib-meningitis costs upwards of \$38,000 depending on the severity of the disease.
- NIH-supported researchers started a company and successfully moved Hib and other experimental vaccines through the full product development pipeline.



For children born in 2009 alone, Hib vaccination saves **\$3.7 billion** annually, including more than **\$1.8 billion** in direct treatment costs.

KNOWLEDGE

- Hib vaccine research provided fundamental understanding of how the infant immune system works, stimulating new strategies for developing effective vaccines for infants.
- The Hib conjugate vaccine technology has been applied to **create several other vaccines against disease-causing bacteria**, such as pneumococci, meningococci, Salmonella typhi, group B streptococci, and E coli.



HIB DISEASE NEARLY ELIMINATED IN THE U.S. FOLLOWING THE VACCINE

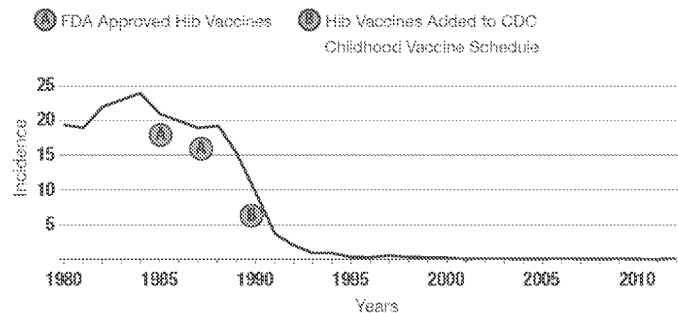


Figure Legend: The CDC-estimated annual incidence of invasive Hib disease (per 100,000 people) is shown here for U.S. children less than five years of age from 1980 to 2012. Once approved and licensed, the use of Hib vaccines resulted in a rapid decline of Hib cases and the disease has been nearly eliminated in the United States.

HEALTH IMPACT OF ROUTINE CHILDHOOD IMMUNIZATION FOR Hib: U.S. 1994-2013

Illnesses Prevented:	Hospitalizations Averted:	Deaths Avoided:
361,000	334,000	13,700

RELATED RESOURCES ON HIB AND OTHER VACCINES

[CDC's Child, Adolescent, & "Catch-up" Immunization Schedules](#)

[CDC's Vaccines for Children Program](#)

[NIAID Health and Research Topics: Vaccines](#)

CHILDHOOD VACCINES: OVERALL IMPACT ON SOCIETY

The Hib vaccine success story highlights how continued scientific investment from the earliest phases of basic research by NIH and others eventually leads to new tools that prevent deadly diseases and improve the lives of people around the world. The Hib vaccine is one of many childhood vaccines that together are estimated to:

save
33,000
lives

prevent
14 million
cases of disease

reduce direct
health care costs by
\$10 billion

save **\$43 billion**
in indirect costs every year
in the United States

For references, supplementary information, and more Research Impact Reports, please visit <http://www.nih.gov/about-nih/what-we-do/impact-nih-research>.

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

From: Girards, Richard (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=6F43C30C4A364463BF5B2C134225B7F0-GIRARDSRT]
Sent: 11/14/2017 7:59:18 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: revised draft
Attachments: Capstone Project submission as of 14 November 2017.docx

Dear Mark-

Thanks for your helpful comments last week.

I have revised the document:

b6

If you're comfortable with this new version, I'll go admit and submit. Barring any major suggestions on your part, I believe that this current version meets the requirements of the course. While I'm not exactly certain what the procedures are, Steve Ferguson and/or Fred Provorny might require some sort of certification from you as to the fact that we've discussed this project and that you generally approve of its form and content- I'll be sure to let you know.

Thanks again!

-Rick

Richard T. Girards, Jr., Esq., MBA
National Institutes of Health
NCI Technology Transfer Center
9609 Medical Center Drive, Room 1E508 MSC 9702
Rockville, MD 20850-9702 *for UPS/FedEx/visitors*
Bethesda, MD 20892-9702 *for U.S. Mail*
richard.girards@nih.gov
Phone: 240-276-6825
Fax: 240-276-5504
<http://ttc.nci.nih.gov>

b6

b6

b6

b6

b6

b6

b6

b6

b6

b6

b6

b6

b6

b6

b6

b6

From: Petrik, Amy (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=C4EC05A179F04067B61F20605E911E7C-PETRIKA]
Sent: 12/13/2017 7:30:20 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]
CC: Salata, Carol (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f98ca6a1f9fc4cfdbbf4036ca8cbace4-csalata]; Feliccia, Vincent (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7f3a54860cb941c1abe1df786e478e00-vfeliccia]
Subject: Final Determination for A-419-2017 for review
Attachments: A-419-2017_FD_13Dec.docx

Hi Mark and Dale,

I've drafted the attached final determination for the proposed PaxVax exclusive license to the NIAID Zika vaccine technology, with input from my TTIPO colleagues.

Would you each, please, review and let me know if you have any suggestions/edits to improve it?

If you have any questions, please don't hesitate to call.

Thanks,

Amy

Amy F. Petrik, Ph.D.
Technology Transfer and Patent Specialist
Technology Transfer and Intellectual Property Office
National Institute of Allergy and Infectious Diseases
National Institutes of Health, HHS

5601 Fishers Lane
Suite 2G
Rockville, MD 20892-9804
240-627-3721

b5

b5

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 5/28/2019 2:33:51 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Wong, Jennifer (NIH/NIMH) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c4258c7cf58f4945a3df079942c68852-wongje]
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics
Attachments: Response to FR notice comments from KEI_MLR--OGCBerkleyComments.docx

Sorry for the delay, good work Jennifer and great comments from Mark
[b5] for your consideration in the attached.

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Friday, May 24, 2019 4:23 PM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, May 24, 2019 4:23 PM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Thanks Jenny. Looks good. I made a few proposed edits. Dale?

From: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Sent: Friday, May 24, 2019 3:47 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Hi all,

Attached is a draft response -- please feel free to modify.

[b5]

Many thanks,
Jenny

Jennifer Wong, M.S.
Technology Development Coordinator
National Institute of Mental Health
Office of Technology Transfer
35A Convent Drive, Room GE400
Bethesda, MD 20892-3747

REL0000024299

Phone: 301-480-4821
E-mail: wongje@mail.nih.gov

Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, dissemination, distribution, copying, use of this email or information enclosed therein is strictly prohibited. If you have received this email in error, please notify the sender and destroy the message and any attachments without making a copy. Thank you.

From: Wong, Jennifer (NIH/NIMH) [E]
Sent: Wednesday, May 22, 2019 12:53 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Great! I'll send out a meeting invite with a call-in number.

Thanks,
Jenny

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, May 22, 2019 10:55 AM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Me too

From: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Sent: Wednesday, May 22, 2019 10:54 AM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Good for me

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Sent: Wednesday, May 22, 2019 10:52 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Hi,

How about 1:30 pm?

Thanks,
Jenny

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, May 21, 2019 5:07 PM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

REL0000024299

I can do Friday after 1

From: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>

Sent: Tuesday, May 21, 2019 4:50 PM

To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>

Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Oh I see that I'll be in route to downtown at that time. You guys go ahead without me, or I could join any time Friday.

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>

Sent: Tuesday, May 21, 2019 2:26 PM

To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>

Cc: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>

Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Hi Mark,

Thursday between 2-4 pm is good. Please let me know when it would be convenient to chat.

b5

b5
additional comments.

when KEI sent the

Thanks,
Jenny

From: Rohrbaugh, Mark (NIH/OD) [E]

Sent: Tuesday, May 21, 2019 11:29 AM

To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>

Cc: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>

Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

b5

Dale will join us if he is available to talk. Would Thursday after 2 work?

From: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>

Sent: Tuesday, May 21, 2019 9:15 AM

To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>

Subject: FW: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Hi Mark,

Are you available to discuss?

Thanks,
Jenny

REL0000024299

Jennifer Wong, M.S.
Technology Development Coordinator
National Institute of Mental Health
Office of Technology Transfer
35A Convent Drive, Room GE400
Bethesda, MD 20892-3747
Phone: 301-480-4821
E-mail: wongje@mail.nih.gov

Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, dissemination, distribution, copying, use of this email or information enclosed therein is strictly prohibited. If you have received this email in error, please notify the sender and destroy the message and any attachments without making a copy. Thank you.

From: Luis Gil Abinader <luis.gil.abinader@keionline.org>
Sent: Monday, May 20, 2019 4:51 PM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Cc: claire.cassedy@keionline.org; Jamie Love <james.love@keionline.org>
Subject: 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Dear Jennifer Wong, MS,

Attached please find the comments by KEI and James Love as an individual with regards to the license proposed in the Federal Register notice 84 FR 19090 to Repurposed Therapeutics, Inc.

Best regards,

Luis Gil Abinader

b5

b5

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 5/16/2018 2:53:57 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: What was NIH response to KEI?????

Will discuss within OPERA.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, May 16, 2018 10:51 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: Re: What was NIH response to KEI?????

b5

Sent from my iPhone

On May 16, 2018, at 9:46 AM, Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov> wrote:

Request from KEI to OTT and DEITR, to discuss with KEI the policies and regulations for transfers to subsidiaries and "off-shore" development.

From: Hammersla, Ann (NIH/OD) [E]
Sent: Wednesday, May 16, 2018 9:29 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: What was NIH response to KEI?????

You were working with Communications about KEI's request to meet on compliance issues

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, May 16, 2018 9:28 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: Re: What was NIH response to KEI?????

On what? I do not recall a recent response

Sent from my iPhone

On May 16, 2018, at 9:24 AM, Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov> wrote:

--

Ann M. Hammersla, J.D.
Director
Division of Extramural Inventions and Technology Resources
Office of Policy for Extramural Research Administration
Rockledge 1, Suite 310
6705 Rockledge Drive

REL0000024300

Bethesda, Maryland 20892-7974
PHONE: 301-435-0745

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 8/2/2018 6:50:29 PM
To: Allen-Gifford, Patrice (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=67262490d6d441b48efec1aff0700250-allengiffor]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Gale, Jamie (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8c7c93b348c44d9a824ced1ecd6b9ae6-galejr]; Hurlebaus, Lisa (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ae3ee4a34a70491ebc62f0caf81d729c-lmarshal]; Crone, Colleen (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8d180cb0cb7d4bdaa8c86d118520b72d-cronec]; Ellis, Chelsea (NIH/OD) [C] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=55244440fa5b4a8a9028147f7e19cc2e-elliscm]
Subject: RE: Vizamyl

Patrice: [REDACTED] b5

[REDACTED] b5

Ann

From: Allen-Gifford, Patrice (NIH/OD) [E]
Sent: Thursday, August 02, 2018 2:45 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Gale, Jamie (NIH/OD) [E] <jamie.gale@nih.gov>; Hurlebaus, Lisa (NIH/OD) [E] <marshall@od.nih.gov>; Crone, Colleen (NIH/OD) [E] <cronec@od.nih.gov>; Ellis, Chelsea (NIH/OD) [C] <chelsea.ellis@nih.gov>
Subject: RE: Vizamyl

Hi Ann,

[REDACTED] b5

Patrice

From: Hammersla, Ann (NIH/OD) [E]
Sent: Thursday, August 02, 2018 2:42 PM
To: Allen-Gifford, Patrice (NIH/OD) [E] <patrice.allen-gifford@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Gale, Jamie (NIH/OD) [E] <jamie.gale@nih.gov>; Hurlebaus, Lisa (NIH/OD) [E] <marshall@od.nih.gov>; Crone, Colleen (NIH/OD) [E] <cronec@od.nih.gov>; Ellis, Chelsea (NIH/OD) [C] <chelsea.ellis@nih.gov>
Subject: RE: Vizamyl

Hello Patrice: Thank you for checking on this. [REDACTED] b5

[REDACTED] b5

Ann

REL0000024301

--

Ann M. Hammersla, J.D.
Director
Division of Extramural Inventions and Technology Resources
Office of Policy for Extramural Research Administration
Rockledge 1, Suite 310
6705 Rockledge Drive
Bethesda, Maryland 20892-7974
PHONE: 301-435-0745

From: Allen-Gifford, Patrice (NIH/OD) [E]
Sent: Thursday, August 02, 2018 2:35 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Gale, Jamie (NIH/OD) [E] <jamie.gale@nih.gov>; Hurlebaus, Lisa (NIH/OD) [E] <marshall@od.nih.gov>; Crone, Colleen (NIH/OD) [E] <cronec@od.nih.gov>; Ellis, Chelsea (NIH/OD) [C] <chelsea.ellis@nih.gov>
Subject: RE: Vizamyl

Hi Mark and Ann,

b5

Please let me know if you need us to follow up.

Best,
Patrice

Patrice Allen-Gifford
Director
Executive Secretariat
301-496-3976

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, August 02, 2018 1:28 PM
To: Allen-Gifford, Patrice (NIH/OD) [E] <patrice.allen-gifford@nih.gov>
Cc: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: FW: Vizamyl

Patrice:

b5

It was sent 5/18

Thanks,
Mark

From: Hammersla, Ann (NIH/OD) [E]
Sent: Thursday, August 02, 2018 1:26 PM

REL0000024301

To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>

Subject: FW: Vizamyl

Collins and I were copied on the KEI request.

From: Hammersla, Ann (NIH/OD) [E]

Sent: Thursday, August 02, 2018 1:25 PM

To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>

Subject: Vizamyl

Mark: On 5/18/2018 KEI sent to Secretary Azar a request to march-in on Vizamyl.

b5

b5

Ann

--

Ann M. Hammersla, J.D.

Director

Division of Extramural Inventions and Technology Resources

Office of Policy for Extramural Research Administration

Rockledge 1, Suite 310

6705 Rockledge Drive

Bethesda, Maryland 20892-7974

PHONE: 301-435-0745

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 1/23/2019 5:51:51 PM
To: Mowatt, Michael (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb1ef7e2e54b4164ae34814574bda638-mmowatt]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]; Soukas, Peter (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b1f6020157ac47948c6e34166b78e433-soukasp]; Williams, Richard (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e5f89fe4d27a43abb936bb20efeca3b9-rwilliams]; Puglielli, Maryann (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9f53ceacaf754875a948081bac5cc66a-pugliellim]
Subject: RE: KEI Response Letter
Attachments: Response to KEI J Love Comments_to DB and MR Jan 10--OGCBerkleyComments--1-23-2019--clean.docx

b5

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

-----Original Message-----

From: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Sent: Tuesday, January 22, 2019 12:53 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>; Soukas, Peter (NIH/NIAID) [E] <peter.soukas@nih.gov>; Williams, Richard (NIH/NIAID) [E] <rwilliams@niaid.nih.gov>; Puglielli, Maryann (NIH/NIAID) [E] <maryann.puglielli@nih.gov>
Cc: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Subject: RE: KEI Response Letter

Team,

I ran into Dale just now at NIH.

b5

b5

we shouldn't need more than 15 or 30 minutes tomorrow.

Thanks Dale and everyone,

Mike

-----Original Message-----

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Tuesday, January 22, 2019 12:24 PM
To: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Cc: Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>; Soukas, Peter (NIH/NIAID) [E] <peter.soukas@nih.gov>; Williams, Richard (NIH/NIAID) [E] <rwilliams@niaid.nih.gov>; Puglielli, Maryann (NIH/NIAID) [E] <maryann.puglielli@nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: Re: KEI Response Letter

Just saw this. Do you have time now?

Sent from my iPhone

> On Jan 22, 2019, at 11:59 AM, Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov> wrote:

> **b6**
> **b6**
> Leader - **b6**
> Participant - **b6**
>

REL0000024302

>
> Thanks, Mary.
>
> This one is a priority, so please squeeze it in this week. Tomorrow afternoon?
>
>
>
> Dear Mary,
>
> We are just following up, we hope everything is going well with you.
>
> Does Mike have any time this week to discuss these issues with Mark Rohrbaugh and Dale Berkley?
>
> We look forward to a meeting invitation soon.
>
> Thank you.
>
> Peter
> <meeting.ics>

b5

b5

b5

From: Lambertson, David (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=3C95B34F709746A8A2553CE54E74ACE2-LAMBERTSOND]
Sent: 9/11/2017 7:22:30 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Rodriguez, Richard (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8092cb5394e04733ac0d4d84d25f65e5-rodrigr]
CC: Whitney, Laurie (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=903a0f2d510b4ef3a081c10eef17deb8-whitneyl]
Subject: RE: Responses to Objecting Comments for A-381-2017

Ok, thanks.

b5

b5

David A. Lambertson, Ph.D.
Senior Technology Transfer Manager
Technology Transfer Center
National Cancer Institute/NIH
david.lambertson@nih.gov
<http://ttc.nci.nih.gov/>

9609 Medical Center Drive, Rm 1-E530 MSC 9702
Bethesda, MD 20892-9702 (USPS)
Rockville, MD 20850-9702 (Overnight/express mail)
Phone (Main Office): 240-276-5530
Phone (direct): (240) 276-6467
Fax: 240-276-5504

Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, copying or use of this email or the information enclosed therein is strictly prohibited, and you should notify the sender for return of any attached documents

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, September 11, 2017 3:20 PM
To: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>; Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Cc: Whitney, Laurie (NIH/NCI) [E] <whitneyl@mail.nih.gov>
Subject: RE: Responses to Objecting Comments for A-381-2017

b5

Happy to review the final.

Thanks
Mark

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, September 11, 2017 10:44 AM
To: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>; Rodriguez, Richard (NIH/NCI) [E]

REL0000024303

<richard.rodriguez@nih.gov>

Cc: Whitney, Laurie (NIH/NCI) [E] <whitneyl@mail.nih.gov>

Subject: RE: Responses to Objecting Comments for A-381-2017

I am working on that and will get back to you today.

From: Lambertson, David (NIH/NCI) [E]

Sent: Monday, September 11, 2017 10:43 AM

To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>

Cc: Whitney, Laurie (NIH/NCI) [E] <whitneyl@mail.nih.gov>

Subject: RE: Responses to Objecting Comments for A-381-2017

Thanks. My initial question was

b5

b5

Please let

us know the preference.

Thanks,

David A. Lambertson, Ph.D.

Senior Technology Transfer Manager

Technology Transfer Center

National Cancer Institute/NIH

david.lambertson@nih.gov

<http://ttc.nci.nih.gov/>

9609 Medical Center Drive, Rm 1-E530 MSC 9702

Bethesda, MD 20892-9702 (USPS)

Rockville, MD 20850-9702 (Overnight/express mail)

Phone (Main Office): 240-276-5530

Phone (direct): (240) 276-6467

Fax: 240-276-5504

Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, copying or use of this email or the information enclosed therein is strictly prohibited, and you should notify the sender for return of any attached documents

From: Rohrbaugh, Mark (NIH/OD) [E]

Sent: Monday, September 11, 2017 10:41 AM

To: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>

Cc: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>; Whitney, Laurie (NIH/NCI) [E] <whitneyl@mail.nih.gov>

Subject: RE: Responses to Objecting Comments for A-381-2017

This is what OD/OC is using for public inquiries.

From: Rodriguez, Richard (NIH/NCI) [E]

Sent: Monday, September 11, 2017 10:17 AM

To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>

Cc: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>; Whitney, Laurie (NIH/NCI) [E] <whitneyl@mail.nih.gov>

REL0000024303

Subject: FW: Responses to Objecting Comments for A-381-2017

Importance: High

Hi Mark,

I'm following up on this question from Dave Lambertson.

b5

b5

I'm copying Dave and Laurie

Whitney.

b5

so if you can get him a quick response, it would be much appreciated.

Thanks,

Richard

From: Lambertson, David (NIH/NCI) [E]

Sent: Tuesday, September 05, 2017 6:54 AM

To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>

Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Whitney, Laurie (NIH/NCI) [E] <whitneyl@mail.nih.gov>

Subject: FW: Responses to Objecting Comments for A-381-2017

Good morning Mark,

I am following up on my e-mail from a couple of weeks ago.

b5

b5

Thanks,

Dave

David A. Lambertson, Ph.D.

Senior Technology Transfer Manager

Technology Transfer Center

National Cancer Institute/NIH

david.lambertson@nih.gov

<http://ttc.nci.nih.gov/>

9609 Medical Center Drive, Rm 1-E530 MSC 9702

Bethesda, MD 20892-9702 (USPS)

Rockville, MD 20850-9702 (Overnight/express mail)

Phone (Main Office): 240-276-5530

Phone (direct): (240) 276-6467

Fax: 240-276-5504

Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, copying or use of this email or the information enclosed therein is strictly prohibited, and you should notify the sender for return of any attached documents

REL0000024303

From: Lambertson, David (NIH/NCI) [E]
Sent: Wednesday, August 23, 2017 7:57 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: Responses to Objecting Comments for A-381-2017

Good morning Mark,

The fifteen (15) day period for objections to the Notice of Intent to Grant for license application A-381-2017 ended last night. There were eight (8) total objections, seven (7) of which were in the form of comments (the eighth was a competing application which will be analyzed and addressed separately in a Final Determination). I have attached the objecting comments that I received to this e-mail for your review. Here is a list of the commenters in order of the date of their submission, for ease of reference:

- 1) Knowledge Ecology International (KEI)
- 2) Samer Nuwayhid
- 3) David Kolstedt
- 4) Bruce Korb
- 5) Arnold Shugarman
- 6) Brinsley Davis
- 7) Paul Stumpf

Richard wanted me to contact you about providing formal responses to the objecting comments concerning our advertisement of intent to grant, particularly in view of the recent article concerning the intent to grant. My initial thought is [REDACTED] b5

[REDACTED] b5

[REDACTED] b5 and send each to your attention for review and comment prior to sending them.

Thanks,
Dave

David A. Lambertson, Ph.D.
Senior Technology Transfer Manager
Technology Transfer Center
National Cancer Institute/NIH
david.lambertson@nih.gov
<http://ttc.nci.nih.gov/>

9609 Medical Center Drive, Rm 1-E530 MSC 9702
Bethesda, MD 20892-9702 (USPS)
Rockville, MD 20850-9702 (Overnight/express mail)
Phone (Main Office): 240-276-5530
Phone (direct): (240) 276-6467
Fax: 240-276-5504

Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, copying or use of this email or the information enclosed therein is strictly prohibited, and you should notify the sender for return of any attached documents

REL0000024303

From: Joe Allen [jallen@allen-assoc.com]
Sent: 11/15/2017 9:37:47 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: Re: FW: TTIP0 FYI - FW: CQ on Zika vaccine

Thanks, hadn't seen this one.

On 11/15/2017 3:28 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:

CQ has now published their story:

NIH Pushes Back on Zika Vaccine Conflict Allegation

The government's premier medical research agency is refuting allegations that its choice to help bring a Zika vaccine to market was a conflict of interest.

For more than a year, the National Institutes of Health has been ushering a Zika vaccine through clinical testing around the world. In October, it announced that it was planning to grant an exclusive license to California-based PaxVax, Inc., a small pharmaceutical company that specializes in vaccines, to further develop the product and eventually bring it to market.

But Ken Kelley, the founder and former chief executive of PaxVax, is currently an adviser in the vaccine research center at the National Institute for Allergy and Infectious Diseases, the NIH division that has been researching the Zika vaccine.

The NIH defended its choice on Wednesday after public health groups earlier this week wrote in opposition to the exclusive license, pointing out Kelley's connection. The NIAID released a statement noting that no other company had submitted an application to license the vaccine.

"NIAID's intent to license the Zika vaccine candidate to PaxVax was based solely on the merits of the company's application and nothing else," the statement said. "With regard to Mr. Kelley, there was and is no conflict of interest. Discussions related to a license application were conducted between PaxVax and NIAID's Technology Transfer and Intellectual Property Office; Mr. Kelley was not involved in those discussions, and he is not involved in decisions to grant licenses."

The groups Doctors Without Borders and Knowledge Ecology International argued the exclusive license could mean that if the vaccine is ultimately for sale, it will be unaffordable for the vulnerable populations who could benefit from it most.

"PaxVax has a history of marketing vaccines to travelers and tourists, and may not be willing or able to scale access in countries where the need is the greatest," the groups said in comments to the NIH.

They also believe that the arrangement is a bad deal for the United States, which has already spent hundreds of millions of dollars on Zika vaccine research. If the vaccine is ultimately approved for use, the company would not only benefit from its sale. Because there are no other treatments for Zika, it could also get tax credits to cover half the cost of its research investment. The company could also win a voucher to bring another product to market more quickly, which it could sell for millions of dollars.

If the NIH finalizes its decision to grant an exclusive license, the groups said it should make PaxVax agree to make it affordable in the U.S. and elsewhere.

Earlier, however, NIAID leader Anthony Fauci told CQ he wasn't worried about price being an issue.

"I have not seen in my experience, situations in which we were involved in the development of a vaccine, particularly for low- and middle-income countries that really needed it, where the pharmaceutical companies priced it out of their reach," he said in an October interview.

The public health groups also noted that the company is now mostly owned by Cerberus Capital Management, whose CEO, they said, donated \$2.2 million to President Donald Trump's campaign and other groups supporting the Trump candidacy.

Earlier this year, a similar licensing arrangement between the government and drug company Sanofi Pasteur for a Zika vaccine developed by the Army was also criticized by public health groups.

Sanofi eventually dropped out of the deal when a separate government funding stream for the Zika research was cut off.

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

From: Joe Allen [jallen@allen-assoc.com]
Sent: 12/12/2017 3:39:28 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]
Subject: KEI: Collins falsely denies B-D march in for high drug prices

FYI: <https://www.keionline.org/23619/>

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(C) [REDACTED] b6
www.allen-assoc.com

From: Wojtowicz, Emma (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=WOJTOWICZEME6D]
Sent: 8/30/2016 12:43:40 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]
CC: Myles, Renate (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=recipients/cn=mylesr]; Fine, Amanda (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Fineab]
Subject: RE: Canadian media question?

Thanks, Mark and Ann. Have a good day.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, August 30, 2016 8:17 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: Re: Canadian media question?

Go with it

Sent from my iPhone

On Aug 30, 2016, at 7:13 AM, Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov> wrote:

Good Morning:

The response is ok with me.

Ann

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, August 29, 2016 4:48 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: FW: Canadian media question?

Ok with you?

From: Wojtowicz, Emma (NIH/OD) [E]
Sent: Monday, August 29, 2016 2:33 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Myles, Renate (NIH/OD) [E] <mylesr@od.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Subject: FW: Canadian media question?

Hi Mark-

We received an inquiry from the Canadian Broadcasting Corporation about march-in rights and Xtandi. We wanted to run our response by you to see if anything has changed since June. Please let us know if you have any edits or concerns.

Response:

REL0000024310

b5

Thank you-
Emma

From: Kelly Crowe [<mailto:kelly.crowe@cbc.ca>]

Sent: Monday, August 29, 2016 1:52 PM

To: Myles, Renate (NIH/OD) [E] <mylesr@od.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>

Subject: Canadian media question?

Hello

My name is Kelly Crowe and I am a medical sciences correspondent with the Canadian Broadcasting Corporation, National News, in Toronto.

I am writing to ask for a comment from the NIH about an offer by a Canadian pharmaceutical company, Biolyse Pharma Corporation, to manufacture the prostate cancer drug Xtandi (enzalutamide) at a reduce price.

I have attached the letter Biolyse wrote to Dr. Frances Collins, in April. I would also appreciate a comment on the NIH response to Knowledge Ecology International, which petitioned the NIH to exercise its march-in rights, or royalty-free rights on enzalutamide. I have attached the letter to the NIH director from Andrew Goldman, along with Dr. Collins' response.

My question concerns the NIH decision to decline the opportunity to have the drug manufactured and supplied at a more affordable price. Why did the NIH turn down this opportunity? Has the NIH ever exercised its march-in or royalty-free rights on any drug? Is the NIH reconsidering the offer from Biolyse, or the petition from Knowledge Ecology International?

I am filing a story tomorrow on the Canadian company's offer to make the drug at a more affordable price, and I would appreciate a comment from the NIH about their offer, and about Knowledge Ecology International's petition.

I appreciate any assistance you can offer.

Thank you

Kelly Crowe

REL0000024310

Medical Sciences Correspondent

CBC National News

416-205-2539 (desk)

b6 (cell)

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 5/15/2018 7:35:05 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

I am working with the program officers on Dr. Griffin's grants.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, May 09, 2018 3:39 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

b5

What are your next steps?

From: Hammersla, Ann (NIH/OD) [E]
Sent: Wednesday, May 09, 2018 9:37 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: FW: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

Mark:

The attached are DFCI's comments regarding the KEI request.

Ann

From: Sclar, Gary M. <Gary_Sclar@DFCI.HARVARD.EDU>
Sent: Wednesday, April 25, 2018 3:00 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Rice Ackman, Rachel E. <Rachel_RiceAckman@DFCI.HARVARD.EDU>; Libka, Hilary <Hilary_Libka@DFCI.HARVARD.EDU>
Subject: RE: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

Dear Ms. Hammersla,

Attached please find the details of our evaluation of the above-referenced patents and NIH Grants P01 CA066996 and RC1 CA147386, as you requested.

As a result of our evaluation, DFCI appropriately did not report that federal funding was used in the conception or reduction to practice of the subject matter of the patents. We are happy to set up a call to discuss further, if this would be useful to you.

Regards,

Gary

REL0000024312

Gary M. Sclar, J.D.
Vice President, Dana-Farber Innovations
Dana-Farber Cancer Institute
Belfer Office for Dana-Farber Innovation
450 Brookline Ave., Boston, MA 02215
Phone: 617-632-5807 • Fax: 617-632-4012
Email: gary_sclar@dfci.harvard.edu

From: Sclar, Gary M.
Sent: Thursday, April 12, 2018 1:59 PM
To: 'Hammersla, Ann (NIH/OD) [E]' <hammerslaa@mail.nih.gov>
Cc: Rice Ackman, Rachel E. <Rachel_RiceAckman@DFCI.HARVARD.EDU>; Libka, Hilary <Hilary_Libka@DFCI.HARVARD.EDU>
Subject: RE: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

Dear Ms. Hammersla,

Thank you for your email. DFCI is aware of KEI's concerns related to grants P01 CA066996 and RC1 CA147386. We have been reviewing this matter internally and plan to provide you with the results of that evaluation by April 25, 2018, as requested.

Regards,

Gary

Gary M. Sclar, J.D.
Vice President, Dana-Farber Innovations
Dana-Farber Cancer Institute
Belfer Office for Dana-Farber Innovation
450 Brookline Ave., Boston, MA 02215
Phone: 617-632-5807 • Fax: 617-632-4012
Email: gary_sclar@dfci.harvard.edu

From: Hammersla, Ann (NIH/OD) [E] [<mailto:hammerslaa@mail.nih.gov>]
Sent: Thursday, April 12, 2018 8:33 AM
To: Sclar, Gary M. <Gary_Sclar@DFCI.HARVARD.EDU>
Subject: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

Dear Mr. Sclar:

On March 21, 2018 Knowledge Ecology International (KEI) brought to the National Institutes (NIH) attention its findings that NIH funding to the Dana-Farber Cancer Institute (Dana-Farber) for Dr. James Griffin was used in the development of the inventions that led to two United States patents referenced above. These patents identify Dr. Griffin as an inventor and were issued jointly to Dana-Farber and Novartis AG. The Food and Drug Administration's Orange Book identifies these patents as being used in the manufacture of Rydapt® (INN midostaurin).

Two NIH grants, P01 CA066996 and RC1 CA147386, have been identified as sources of research funding that may have led to the conception or the reduction to practice of the subject inventions that led to these two patents. Dana Farber disclosed to NIH 18 subject inventions in iEdison with Dr. Griffin as an inventor but has not reported the issuance of these two identified patents.

KEI, in its attached March 21, 2018 letter requests that NIH take title to these two identified patents in accordance with 37 C.F.R. § 401.14(a)(d), require U.S. Manufacturing as required by 37 C.F.R. § 401.14(a)(i), and/or or based on NIH's findings of Dana-Farber's lack of compliance in disclosing or acknowledging NIH support of the two patents in question use NIH's rights as set forth at 37 C.F.R. § 401.14(a)(j).

As part of the NIH's Bayh-Dole Act oversight responsibilities, NIH requests that within ten business days of the date of this email, Dana-Farber provide detailed information concerning NIH's research funding to Dana-Farber for research by Dr. Griffin, including the two NIH grants cited above, and its evaluation of whether federal funding was used in the conception or reduction to practice of the inventions that led to the granting of these two patents.

If you have any questions, you can contact me at the number and email address below.

Ann Hammersla

--

Ann M. Hammersla, J.D.

Director

Division of Extramural Inventions and Technology Resources

Office of Policy for Extramural Research Administration

Rockledge 1, Suite 310

6705 Rockledge Drive

Bethesda, Maryland 20892-7974

PHONE: 301-435-0745

The information in this e-mail is intended only for the person to whom it is addressed. If you believe this e-mail was sent to you in error and the e-mail contains patient information, please contact the Partners Compliance HelpLine at <http://www.partners.org/complianceline> . If the e-mail was sent to you in error but does not contain patient information, please contact the sender and properly dispose of the e-mail.

From: Vepa, Sury (NIH/NCATS) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=25B6C29F123544738FCBAD51627B2D23-VEPAS]
Sent: 8/1/2018 4:00:21 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Portilla, Lili (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9b03f548be224eb9b7b6167a32e9cc4a-portilll]
Subject: FW: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

FYI

Sury

Phone: 301-827-7181
Cell: b6
E-Mail: sury.vepa@nih.gov

From: Vepa, Sury (NIH/NCATS) [E]
Sent: Wednesday, August 1, 2018 11:59 AM
To: 'James Love' <james.love@keionline.org>
Cc: Luis Gil Abinader <luis.gil.abinader@keionline.org>; Claire Cassedy <claire.cassedy@keionline.org>; Manon Ress <manon.ress@keionline.org>; Thiru Balasubramaniam <thiru@keionline.org>
Subject: RE: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

VIA E-MAIL ONLY

James Love
Knowledge Ecology International
1621 Connecticut Ave. NW, Suite 500
Washington, DC 20009

Re: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

Dear Mr. Love,

Thank you for your emails dated July 10, 2018 regarding the prospective grant of an exclusive license to Apexx Oncology, which was published on June 25, 2018 in the Federal Register (83 FR 29562). The notice period provides an opportunity for public comment and possible objection to the proposed license. We consider all comments prior to negotiating the proposed license.

Specifically, we have considered your comments and address them in the following:

1. With respect to your comments about the license applicant, Apexx Oncology, Inc. (f/k/a FBIO Acquisition Corp. VI) is a majority-owned subsidiary of Fortress Biotech, Inc., a biopharmaceutical company dedicated to acquiring, developing and commercializing novel pharmaceutical and biotechnology products, both at the Fortress level and within certain of its subsidiaries, also known as Fortress Companies (<http://www.fortressbiotech.com>). Regarding its corporate details and business plans etc., we are unable to provide that information as we

have learnt that information solely from the license application and as such it is privileged and confidential and is not subject to disclosure under 5 USC §552.

2. Regarding your comment “did the NIH have no reasonable prospects for a license to an entity with more resources and a stronger track record than a company that seems to barely exist,” prior to posting this notice for a proposed grant of an exclusive license, the NCATS determined that the criteria set forth in 37 CFR 404.7(a)(1)(ii-iii) have been satisfied and that the company is qualified to be granted an exclusive license to the Government’s intellectual property in the fields of use as specified.
3. With respect to your recommendations regarding pricing of products made by the licensee, NIH has not included pricing provisions in its licenses for many years, for reasons that have been extensively discussed in the literature, which is readily and publicly available.
4. Regarding your recommendation that “the licensee should be required to file an annual report to the NIH, available to the public, on the research and development (R&D) costs associated with the development of any product that uses the invention, including reporting separately and individually the outlays on each clinical trial,” we already require our license applicants/licensees to provide us with sufficient information to evaluate the viability of their commercial plans and to continuously monitor the progress of the development of the licensed technology towards practical application. To the extent that this information is not already publicly available, it is confidential business information and we carefully maintain the confidentiality of that information as required by 37 C.F.R. 404, 5 USC §552 and other applicable regulations and statutes.
5. Regarding your comments about limiting or reducing the exclusivity, those determinations were made prior to the advertisement of the proposed license and consistent with 37 CFR 404.7 and other applicable regulations.

Once again, we thank you for the comments and recommendations provided by the KEI. NCATS has carefully reviewed and given serious consideration to your comments and recommendations. We have determined that KEI’s comments fail to establish that the grant of the prospective license to the Apexx Oncology would be inconsistent with applicable regulatory and statutory requirements. Consistent with NIH licensing practices, NCATS will review and consider all the comments and any objections it has received. If none of these are found to warrant a change in our proposed license, NCATS will proceed with the negotiation of an exclusive license to the Apexx Oncology.

Sincerely,

Sury Vepa

Sury Vepa, Ph.D., J.D.
Senior Licensing and Patenting Manager
National Center for Advancing Translational Sciences, NIH
9800 Medical Center Drive
Rockville, MD 20850
Phone: 301-827-7181
Cell: [REDACTED] b6
Fax: 301-217-5736

E-Mail: sury.vepa@nih.gov
Website: www.ncats.nih.gov

NIH NCATS: Improving Health Through Smarter Science
Connect with us!: <https://ncats.nih.gov/connect>

This e-mail may contain confidential and/or privileged material for the sole use of the intended recipient. Any review or distribution by others is strictly prohibited. If you are not intended recipient please contact the sender and delete all copies of this e-mail.

From: James Love [mailto:james.love@keionline.org]

Sent: Tuesday, July 10, 2018 4:35 PM

To: Vepa, Sury (NIH/NCATS) [E] <sury.vepa@nih.gov>

Cc: Luis Gil Abinader <luis.gil.abinader@keionline.org>; Claire Cassedy <claire.cassedy@keionline.org>; Manon Ress <manon.ress@keionline.org>; Thiru Balasubramaniam <thiru@keionline.org>

Subject: Re: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

July 10, 2018

Sury Vepa, Ph.D., J.D.,
Senior Licensing and Patenting Manager,
National Center for Advancing Translational Sciences
National Institutes of Health
Email sury.vepa@nih.gov

Re: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

<https://www.federalregister.gov/documents/2018/06/25/2018-13486/prospective-grant-of-exclusive-patent-license-mutant-idh1-inhibitors-useful-for-treating-cancer>

Dear Dr. Vepa,

Knowledge Ecology International (KEI) offers the following comments on the, "Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer," to Apexx Oncology, which was noticed in the Federal Register (83 FR 29562).

As far as the public can determine, Apexx Oncology is a secretive startup company. The only information we could find using a Google search about the company was a contest for a logo of the company. There is no record of a registered trademark for Apexx Oncology with the USPTO. No web page has been located. It is not obvious if Apexx Oncology is a new name for GeneXion Oncology (as indicated today), or a new company entirely, and in any case, there is next to nothing generally known about the company under either name.

When the NIH proposes giving an exclusive license on a patent to a company for which almost nothing is known, it should provide at the very least some basic information about the company. In seeking to respond to the first FR notice in this case, we had asked if GeneXion was owned by a company in Switzerland, but the NIH declined to answer. We don't know who is on the board of directors, who the key staff are or if another company owns this company. We would like to know if any current or former NIH employees or contractors are part of the company.

We also seek to learn -- why this company was selected in the first place? Do they have people who have worked on this particular technology, or have some special expertise? And since the patents are fairly new, did the NIH have no reasonable prospects for a license to an entity with more resources and a stronger track record than a company that seems to barely exist?

Here are some general provisions that we recommend for an exclusive license by the NIH.

1. No discrimination against US residents in pricing.

Prices in the U.S. for any drug, vaccine, medical device or other health technology using the invention should not be higher than the median price charged in the seven countries with the largest gross domestic product (GDP), that also have a per capita income of at least 50 percent of the United States, as measured by the World Bank Atlas Method.

2. Developing countries.

The license should not be exclusive for countries with a per capita income that is less than 30 percent of the US.

3. Transparency.

The licensee should be required to file an annual report to the NIH, available to the public, on the research and development (R&D) costs associated with the development of any product that uses the invention, including reporting separately and individually the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward the company be required to report on actual R&D outlays to develop the subject inventions.

4. Reduce term of exclusivity when revenues are large.

The exclusivity of the license in the U.S. should be reduced by one year for every \$500 million in revenue equivalents, earned after the first \$1 billion, where revenue equivalent is defined as global cumulative sales plus market entry rewards as well as government grants or tax credits, for the product or products using the invention.

Sincerely,



James Love
Knowledge Ecology International
james.love@keionline.org
<https://keionline.org>

--

James Love. Knowledge Ecology International
<http://www.keionline.org/donate.html>
KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584,
twitter.com/jamie_love

From: Joe Allen [jallen@allen-assoc.com]
Sent: 12/8/2017 10:14:37 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]
Subject: The government could march in to control drug prices, but won't

An extended version of The Hill article, this one appeared in Above The Law (<https://abovethelaw.com/2017/12/the-government-already-has-the-tools-it-needs-to-make-pharmaceutical-drugs-affordable-if-it-really-wanted-to/>). Obviously, they see the Azar nomination as an opportunity to resurrect the issue

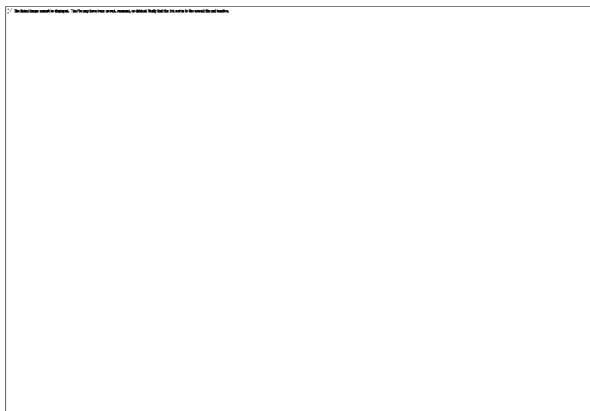
Intellectual Property

The Government Already Has The Tools It Needs To Make Pharmaceutical Drugs Affordable — If It Really Wanted To

The government has never exercised its rights under the Bayh-Dole Act to do so.

By Krista L. Cox

Dec 7, 2017 at 12:22 PM



It's no secret that pharmaceutical drugs can be incredibly expensive. The United States spends more than \$370 billion dollars each year on prescription drugs, more than any other high-income country, clearly contributing to the high costs of health care. Pharmaceutical companies that hold the monopoly rights to patented drugs can charge whatever price they want, or at least whatever the market will bear. Sometimes, this monopoly power means a company will arbitrarily raise the price five-fold overnight simply because it *can*, with no link to actual costs of production or other rationale.

Last week, on November 29, Trump's new nominee for Secretary for the Department of Health and Human Services (HHS), Alex Azar, testified before the Senate Health, Education, Labor and Pensions Committee that prescription drug prices are too high. Azar's nomination has been scrutinized because under his tenure as

president of pharmaceutical giant Eli Lilly, costs of drugs steeply increased, including tripling of the price of insulin. During the hearing, Azar promised to address high drug prices as one of his priorities.

As different strategies to address the drug-pricing crisis are discussed and considered, it is worth remembering that HHS already has the power necessary to reduce the costs for many patented, life-saving medicines through a provision of the Bayh-Dole Act of 1980. And yet, HHS has never exercised these rights, known as “march-in rights,” in the 37 years of the existence of the Bayh-Dole Act.^[1]

These march-in rights were intended to act as safeguards — to ensure that federally funded inventions were being used for the benefit of the public, including being made “available to the public on reasonable terms” or where public health or safety needs are not being satisfied — when the Bayh-Dole Act made it easier for recipients of federal funding to seek patent ownership of federally funded research. The federal government spends billions of dollars each year on research; up to half of all new medicines in the United States are invented at universities through taxpayer funding and it therefore seems reasonable that the public should reap the benefits of publicly funded inventions.

Since the Bayh-Dole clarified the path to patent ownership, however, universities routinely patent taxpayer funded inventions, then exclusively license them to private companies who, in turn, hold monopoly power to price these drugs at whatever they want. While the Bayh-Dole Act was intended to include protections to curb abuses of taxpayer-funded research, in practice these safeguards have not been utilized. As a result, taxpayers are essentially forced to pay for federally funded pharmaceutical inventions twice: once for the underlying research that federal government grants pay for, and again as patients for the costs of the monopoly-priced medicines.

The fact that the NIH/HHS has never exercised their march-in rights in the 37 year history of the Bayh-Dole Act means one of two things: either there have never been any abuses of NIH/HHS-funded patent rights during this time period or that the government doesn’t care enough to actually step in and curb these abuses. The NIH has repeatedly denied requests for the exercise of march-in rights because, despite the fact that the Bayh-Dole Act notes that practical application of an invention means that the invention is being made available “on reasonable terms” the NIH has interpreted this phrase as not including price considerations. In essence, what the NIH has concluded is that as long as an invention is on the market, it is being made available on reasonable terms. A drug company could charge a million dollars for a single pill, but under the NIH’s reasoning, march-in rights would not be warranted.

While Azar testified that lowering drug prices is a priority, Azar’s background as the president of a company that tripled the price of insulin on a whim, the fact that he served as HHS’ general counsel from 2001 to 2005 during which time the NIH (a division of HHS) twice refused to exercise march-in rights on life-saving medicines, and the lack of any exercise of march-in rights by the agency don’t warrant much optimism. Although it would be easy and entirely possible under current law for the government, including HHS, to make many pharmaceutical drugs more affordable, history has shown little appetite for actually using the safeguards that exist under the Bayh-Dole Act.

[1] Full disclosure: I submitted one march-in petition — a second petition on ritonavir in a second petition for ritonavir filed in 2012 on behalf of four NGOs, the American Medical Students Association (AMSA), Knowledge Ecology International (KEI), U.S. Public Interest Research Group (U.S. PIRG), and the Universities Allied for Essential Medicines (UAEM) — which was ultimately rejected. That petition noted that the prices that Abbott was charging for ritonavir in the United States were 4-10 times higher than when compared to other high-income countries, highlighting the absurdity of the system. Not only do taxpayers pay for the underlying research and then again for the product at monopoly prices, but we do so at a much higher cost than our European counterparts.

Krista L. Cox is a policy attorney who has spent her career working for non-profit organizations and associations. She has expertise in copyright, patent, and intellectual property enforcement law, as well as international trade. She currently works for a non-profit member association advocating for balanced copyright. You can reach her at kristay@gmail.com.

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

From: Thomas, Gina (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/CN=OD/CN=GTHOMAS]
Sent: 1/18/2017 10:36:22 PM
To: Kassilke, Deborah (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/cn=od/cn=kassilke]; Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: KEI Request for CRADAs

The list that was attached by Bruce is what OTT provided. I am unsure what Susan Cornell sent. This CRADA was only for our Input.

Gina

From: Kassilke, Deborah (NIH/OD) [E]
Sent: Wednesday, January 18, 2017 5:10 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Thomas, Gina (NIH/OD) [E] <gthomas@od.nih.gov>
Subject: FW: KEI Request for CRADAs

Gina – please advise – do we have the actual information that was submitted to KEI for this foia request back in 2015? It looks like we DID provide a list of CRADAS. See below:

From: Thomas, Gina (NIH/OD) [E]
Sent: Wednesday, January 18, 2017 4:51 PM
To: Rogers, Karen (NIH/OD) [E] <RogersK@od.nih.gov>
Subject: FW: KEI Request for CRADAs

From: Goldstein, Bruce (NIH/OD) [E]
Sent: Tuesday, April 28, 2015 6:27 PM
To: Cornell, Susan (NIH/OD) [E] <CornellS@OD.NIH.GOV>
Cc: Ferguson, Steve (NIH/OD) [E] <FERGUSOS@od6100m1.od.nih.gov>; Thomas, Gina (NIH/OD) [E] <gthomas@od.nih.gov>
Subject: RE: KEI Request for CRADAs

Hi.

Tedious but very easy. I took the liberty of adding the current status of each CRADA, which might be helpful in narrowing their requests. I wasn't sure whether

b5

b5

Regards,
Bruce D. Goldstein, Esq.
NIH Office of Technology Transfer

From: Thomas, Gina (NIH/OD) [E]
Sent: Tuesday, April 28, 2015 4:59 PM
To: Goldstein, Bruce (NIH/OD) [E]
Cc: Ferguson, Steve (NIH/OD) [E]
Subject: FW: KEI Request for CRADAs

Bruce can you please rerun the CRADA report with the items highlighted in yellow only.

b5

Thanks

Gina

From: Cornell, Susan (NIH/OD) [E]
Sent: Tuesday, April 28, 2015 3:19 PM
To: Thomas, Gina (NIH/OD) [E]
Cc: Ferguson, Steve (NIH/OD) [E]; Berkley, Dale (NIH/OD) [E]
Subject: KEI Request for CRADAs

Good Afternoon,

I just got off the phone with Ms. Cassedy of KEI. I explained that NIH has approximately 800 CRADAS and 500 amendments that fall within her timeframe and that our very conservative estimate of a total page count was 45,000 - 50,000 pages (many thanks, Gina, for those numbers!). She said they had no idea there would be that many. I suggested that she take a list of the CRADAs with the CRADA partner, the title and the date signed/executed and she said that would be great. [REDACTED] b5 FYI, that is the same information we provided to Public Citizen 15 years ago.

So, the question is this [REDACTED] b5

[REDACTED] b5

Thanks for your ongoing help with this one!

Susan

Susan R. Cornell, J.D.
Freedom of Information Officer
National Institutes of Health
Building 31, Room 5B35
9000 Rockville Pike
Bethesda, MD 20892

PH: 301-496-5633
FAX: 301-402-4541
EMAIL: cornells@od.nih.gov



REL0000024319

From: Kesselheim, Aaron Seth, M.D., M.P.H. [akesselheim@bwh.harvard.edu]
Sent: 8/1/2018 2:12:26 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: Questions about CRADAs

Great news! A formal invitation will follow shortly -- Looking forward to it, Aaron

-----Original Message-----

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Tuesday, July 31, 2018 7:46 PM
To: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
Subject: Re: Questions about CRADAs

External Email - Use Caution

Aaron:

I am able to attend.

Regards
Mark

Sent from my iPhone

> On Jul 31, 2018, at 1:43 PM, Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu> wrote:
>
> We just sent out some invitations this week and are beginning to discuss it with folks, although since it's the summer, I assume people will be responding slowly. Sounds like [b6] won't be in town, so we're looking for other economists to take her place. Also happy to accept suggestions of names of people who you might think would be useful additions!

>
> Best,
> Aaron
>

> -----Original Message-----

> From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
> Sent: Tuesday, July 31, 2018 1:39 PM
> To: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
> Subject: RE: Questions about CRADAs

>
> External Email - Use Caution

> I am interested. Have there been any additions or subtractions to your list of invitees?

>
> Thanks,
> Mark
>

> -----Original Message-----

> From: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
> Sent: Tuesday, July 31, 2018 1:31 PM
> To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
> Subject: RE: Questions about CRADAs

> Hi Mark -- just following up on this. Any feedback? Or chance we might be able to entice you to join us for one or both days? Best, Aaron

>
> -----Original Message-----

> From: Kesselheim, Aaron Seth, M.D., M.P.H.
> Sent: Thursday, July 19, 2018 5:30 PM
> To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
> Subject: RE: Questions about CRADAs

>
> We hope so. The (at this point, confidential) list of other invitees is below. We would welcome your participation as a member of the conversation throughout the meeting, or for a half-day period, or even as a guest speaker at lunch or dinner. We will operate under 'Chatham House Rules' such that there will be no quotes attributed to anyone.

>
> Let me know what you think! We believe it will be very useful to have your perspective and contribution--

>
> Best,

> Aaron

b6

> -----Original Message-----

> From: Rohrbaugh, Mark (NIH/OD) [E] [mailto:rohrbaum@od.nih.gov]
> Sent: Thursday, July 19, 2018 5:05 PM
> To: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
> Subject: RE: Questions about CRADAs

> External Email - Use Caution

> Aaron:

> I am considering your invitation to the Dec meeting. Will the attendees represent a breadth of thinking and opinions about this issue?

> Thanks
> Mark

> -----Original Message-----

> From: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
> Sent: Wednesday, July 18, 2018 4:05 PM
> To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
> Subject: RE: Questions about CRADAs

> So noted! This is all for our background knowledge. Thanks for responding!

> Any initial thoughts about joining us in Boston for the December event?

> ASK

> -----Original Message-----

> From: Rohrbaugh, Mark (NIH/OD) [E] [mailto:rohrbaum@od.nih.gov]
> Sent: Wednesday, July 18, 2018 4:03 PM
> To: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
> Subject: RE: Questions about CRADAs

> External Email - Use Caution

> Aaron:

> Note that I do not give permission to publish or otherwise publicize my direct comments without permission.

> By the late 1980s, NIH was using one standard model agreement for all types of CRADA collaborations. We noted later that some types of collaborations required fewer terms in this standard agreement. In particular, when the collaboration involved primarily the receipt and training in the use of unique research materials from a company, terms dealing with other matters such as human subjects, reports from the company, regular meetings between the parties, etc. were not relevant and therefore not needed. Rather than send a company lawyer a document with a number of nonrelevant terms to be deleted, NIH developed a M-CRADA stripped down to the terms relevant to or otherwise legally required in a collaboration involving primarily materials. It sped up negotiation and thus benefited both the NIH and the company providing the unique materials.

> Since then other CRADA models were developed to suit particular types of commercial collaborations, e.g. clinical research.

> CRADA partners do not decide on which model, NIH decides.

> -----Original Message-----
> From: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
> Sent: Wednesday, July 18, 2018 11:21 AM
> To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
> Subject: RE: Questions about CRADAs

>
> Thanks Mark! This is very useful--I will read this over. Here are the questions we have, which may not be covered by this overview:

>
> 1. What's the difference between a CRADA and a Materials CRADA (MCRADA)? In particular, are there any cost benefits or differences in accessibility between a CRADA and an MCRADA?
> 2. Prior to 1996 (when the NIH initiated MCRADAs), could any of the signed CRADAs cover what is now included in an MCRADA?
> 3. How do potential CRADA partners decide between a CRADA and a MCRADA?
> 4. What motivated the NIH to introduce the MCRADA mechanism in 1996?

>
> Let me know if this is worth a phone call.

>
> On a different note, we're organizing a Radcliffe Seminar at Harvard this winter (December 11-12) on the subject of government funding of drug development and the different strategies that are currently taken (and that have been proposed) to account for that contribution. It's a small group session of like 15 or so experts in science, economics, law, and medicine from around the country. It would be great to have you join us if not for the whole time, at least as a guest/featured speaker over lunch or dinner -- would something like that be possible?

>
> Best,
> Aaron

> -----Original Message-----
> From: Rohrbaugh, Mark (NIH/OD) [E] [mailto:rohrbaum@od.nih.gov]
> Sent: Wednesday, July 18, 2018 11:16 AM
> To: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
> Subject: RE: Questions about CRADAs

>
> External Email - Use Caution

>
> Here is NIH's overview of CRADAs. <https://www.ott.nih.gov/policy/cradas>

> -----Original Message-----
> From: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
> Sent: Tuesday, July 17, 2018 10:43 PM
> To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
> Subject: Questions about CRADAs

>
> Hi Mark -- hope all is well. One of the people in my research group is doing a project on CRADAs and had a few fundamental questions that I thought you might be able to help with -- would it be ok to send the questions over email, or maybe set up a time to quickly chat?

>
> Best,
> Aaron

>
>
> Aaron S. Kesselheim, M.D., J.D., M.P.H.
> Associate Professor of Medicine at Harvard Medical School Director, Program On Regulation, Therapeutics, And Law (PORTAL) Division of Pharmacoepidemiology and Pharmacoeconomics Brigham and Women's Hospital
> 1620 Tremont St, Suite 3030
> Boston MA 02120
> akesselheim@partners.org
> P: 617-278-0930; F: 617-232-8602
> <http://www.PORTALresearch.org>

>
> Faculty member, Harvard Medical School Center for Bioethics Irving S. Ribicoff Visiting Associate Professor of Law, Yale Law School (2016-2018) Editor-in-Chief, Journal of Law, Medicine, and Ethics

>
> Don't miss our policy and ethics seminar series

>
>
>
>
>
>
>
> The information in this e-mail is intended only for the person to whom it is addressed. If you believe this e-mail was sent to you in error and the e-mail contains patient information, please contact the Partners Compliance HelpLine at <http://www.partners.org/complianceline> . If the e-mail was sent to you in error but does not contain patient information, please contact the sender and properly dispose of the e-mail.

>

>
>
>

From: Barnes, Mary (NIH/NIAID) [C] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=29EEA0C3E3FF40F299BF2EEB40BE91CE-BARNESML]
Sent: 1/22/2019 4:59:43 PM
To: Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]; Soukas, Peter (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b1f6020157ac47948c6e34166b78e433-soukasp]; Williams, Richard (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e5f89fe4d27a43abb936bb20efeca3b9-rwilliams]; Puglielli, Maryann (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9f53ceacaf754875a948081bac5cc66a-pugliellim]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: KEI Response Letter
Location: 5601-6C100
Start: 1/23/2019 6:00:00 PM
End: 1/23/2019 7:00:00 PM
Show Time As: Tentative

Required Attendees: Frisbie, Suzanne (NIH/NIAID) [E]; Soukas, Peter (NIH/NIAID) [E]; Williams, Richard (NIH/NIAID) [E]; Puglielli, Maryann (NIH/NIAID) [E]; Berkley, Dale (NIH/OD) [E]; Rohrbaugh, Mark (NIH/OD) [E]

b6

Leader -

b6

Participant -

b6

Thanks, Mary.

This one is a priority, so please squeeze it in this week. Tomorrow afternoon?

Dear Mary,

We are just following up, we hope everything is going well with you.

Does Mike have any time this week to discuss these issues with Mark Rohrbaugh and Dale Berkley?

We look forward to a meeting invitation soon.

Thank you.

Peter

REL0000024322

From: Routh, Jennifer (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=E3B5BBA3619344E38037CA94A71473A8-ROUTHJ]
Sent: 10/17/2017 7:08:10 PM
To: Mowatt, Michael (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb1ef7e2e54b4164ae34814574bda638-mmowatt]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Stover, Kathy (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c82722674ba14c2f969bd50dfa6a7af4-stoverk]; Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]
Subject: RE: For awareness
Attachments: Questions from Ed Silverman at STAT KS MM.docx

Thanks, Mike. b5 Mark – attached is a clean version. We’re circulating this within NIAID now and plan to send to HHS for clearance this afternoon.

Jennifer Routh [E]
Scientific Communications Editor
Office of Communications and Government Relations
National Institute of Allergy and Infectious Diseases (NIAID)
NIH/HHS
31 Center Drive Room 7A17B
Bethesda, MD 20892
Direct: (301) 496-8327
jennifer.routh@nih.gov

Disclaimer: The information in this e-mail and any of its attachments is confidential and may contain sensitive information. It should not be used by anyone who is not the original intended recipient. If you have received this e-mail in error please inform the sender and delete it from your mailbox or any other storage devices. The National Institute of Allergy and Infectious Diseases shall not accept liability for any statements made that are sender's own and not expressly made on behalf of the NIAID by one of its representatives.

From: Mowatt, Michael (NIH/NIAID) [E]
Sent: Tuesday, October 17, 2017 12:50 PM
To: Routh, Jennifer (NIH/NIAID) [E] <jennifer.routh@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>
Subject: RE: For awareness

See my comments tracked.

Mark will chime in with changes/additions if he has any.

In the future please do not hesitate to specify a deadline when you need our response. It helps us prioritize.

From: Routh, Jennifer (NIH/NIAID) [E]
Sent: Tuesday, October 17, 2017 10:39 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>
Cc: Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>
Subject: RE: For awareness

Mark, Mike and Suzanne –

Thanks for your input. We've drafted a response to the reporter (attached) with a few questions in the margin. Please let us know what you think.

Thanks,
Jen

Jennifer Routh [E]
Scientific Communications Editor
Office of Communications and Government Relations
National Institute of Allergy and Infectious Diseases (NIAID)
NIH/HHS
31 Center Drive Room 7A17B
Bethesda, MD 20892
Direct: (301) 496-8327
jennifer.routh@nih.gov

Disclaimer: The information in this e-mail and any of its attachments is confidential and may contain sensitive information. It should not be used by anyone who is not the original intended recipient. If you have received this e-mail in error please inform the sender and delete it from your mailbox or any other storage devices. The National Institute of Allergy and Infectious Diseases shall not accept liability for any statements made that are sender's own and not expressly made on behalf of the NIAID by one of its representatives.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, October 17, 2017 10:11 AM
To: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>; Billet, Courtney (NIH/NIAID) [E] <billetc@niaid.nih.gov>; Fauci, Anthony (NIH/NIAID) [E] <afauci@niaid.nih.gov>
Cc: Mascola, John (NIH/VRC) [E] <jmascola@mail.nih.gov>; Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>; Routh, Jennifer (NIH/NIAID) [E] <jennifer.routh@nih.gov>; Conrad, Patricia (NIH/NIAID) [E] <conradpa@niaid.nih.gov>; Folkers, Greg (NIH/NIAID) [E] <gfolkers@niaid.nih.gov>
Subject: RE: For awareness

I agree.

b5

b5

From: Mowatt, Michael (NIH/NIAID) [E]
Sent: Tuesday, October 17, 2017 10:05 AM
To: Billet, Courtney (NIH/NIAID) [E] <billetc@niaid.nih.gov>; Fauci, Anthony (NIH/NIAID) [E] <afauci@niaid.nih.gov>
Cc: Mascola, John (NIH/VRC) [E] <jmascola@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>; Routh, Jennifer (NIH/NIAID) [E] <jennifer.routh@nih.gov>; Conrad, Patricia (NIH/NIAID) [E] <conradpa@niaid.nih.gov>; Folkers, Greg (NIH/NIAID) [E] <gfolkers@niaid.nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Subject: RE: For awareness

Regarding Q2:

b5

Having said this, the starting point for the license negotiation will be a publicly available "NIH model" license agreement (see <https://www.ott.nih.gov/resources#MLA>, "Exclusive patent license agreement"), the majority of the terms of which usually remain unmodified. The appendices include the most sensitive information.

Mark may have additional comments.

Mike

REL0000024323

From: Billet, Courtney (NIH/NIAID) [E]
Sent: Tuesday, October 17, 2017 9:05 AM
To: Fauci, Anthony (NIH/NIAID) [E] <afauci@niaid.nih.gov>
Cc: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>; Mascola, John (NIH/VRC) [E] <jmascola@mail.nih.gov>; Rohrbach, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>; Routh, Jennifer (NIH/NIAID) [E] <jennifer.routh@nih.gov>; Conrad, Patricia (NIH/NIAID) [E] <conradpa@niaid.nih.gov>; Folkers, Greg (NIH/NIAID) [E] <gfolkers@niaid.nih.gov>
Subject: For awareness

We have been contacted by STAT's Ed Silverman, author of the piece below from May re Sanofi deal.

We have sent him the Fed Reg notice, and are now working on answers to some follow-up questions, which are (1) why an ***exclusive*** license and (2) assuming we proceed with licensure, will the terms be disclosed. We have the answer to the first question and are seeking the answer to the second. He is not requesting an interview.

<https://www.statnews.com/2017/05/29/zika-vaccine-price/>

US taxpayers are funding a Zika vaccine. Let's make sure US patients can afford it

By ED SILVERMAN
MAY 29, 2017

*D*ear Acting Secretary Speer,

As you know, the United States must prepare for future outbreaks of the Zika virus, but a high-stakes debate has erupted over a deal the federal government may strike with a private company to develop a vaccine. As acting secretary of the US Army, you have an opportunity — and responsibility — to find a workable solution.

The issue is whether the company — in this case, Sanofi Pasteur — should be required to make the vaccine, which is based on technology discovered with US taxpayer funds, affordable for Americans in return for an exclusive license to develop it into a commercial product.

I understand there are risks, but you should find a way to ensure that Americans do not overpay.

Here's the backstory: Last year, the government gave Sanofi, which is one of the world's largest vaccine makers, a \$43 million grant. Another \$130 million may follow as research continues. The Army also disclosed plans to award Sanofi an exclusive license to a pair of patents that are crucial to the vaccine.

But this move upset some lawmakers and patient advocates, who fear the deal will give the company a monopoly to exploit — and might lead Sanofi to jack up prices for American consumers, assuming the virus spreads and vaccines actually become a big market.

The backdrop to such concerns is the larger controversy over the rising cost of prescription medicines, a problem that has upset many Americans, prompted a flurry of legislation, and put the pharmaceutical industry on the defensive.

Sanofi, which is already under fire over its insulin pricing, is well-aware of the problem. Earlier this month, the company sought to deflect criticism — and mounting negative publicity — by vowing to limit price hikes for its medicines to a level at or below the rate of medical inflation in the US.

But an advocacy group, Knowledge Ecology International, argued Sanofi cannot be trusted and pointed to pricing for its Aubagio multiple sclerosis drug. Americans using a coupon can pay about \$6,100 for a month's supply — which is seven times more than patients pay in France and at least four times the price in the UK, Ireland, and Australia. A Sanofi spokeswoman says prices vary due to circumstances in each country.

This is why Senator Bernie Sanders and others maintain the Army should push Sanofi for fair pricing on the Zika vaccine. They want a guarantee that Americans would pay a price comparable to what other countries are charged. But as you know, Secretary Speer, Sanofi rejected such a request from your staff last month.

Drug makers generally avoid discussing pricing decisions in advance and Sanofi is no exception. In this case, the company has noted the vaccine doesn't even exist yet.

A Sanofi executive offered further insight in a letter to a House subcommittee last week. "Given the high risk nature of vaccine development and unpredictability for diseases like Zika, if the US government changes its historic approach to licensing terms, it could undermine the intent of these types of collaborations," wrote Adam Gluck, who heads US government relations for the drug maker.

In other words, if a company is forced to agree to certain pricing constraints in advance, it may not bother working with the government to develop such vaccines in the first place.

Indeed, this risk that companies might respond in this way has long worried government officials. In 1995, in fact, the National Institutes of Health removed what was called a "reasonable pricing" clause from research agreements with companies. At the time, former NIH Director Harold Varmus described such clauses as a "restraint" on new product development.

"What companies don't like is additional uncertainty for commercial considerations piled on top of the inherent risk of doing drug development," said Genia Long, a senior advisor at Analysis Group, an economic and strategic consulting firm. "If the federal government is going to insert pricing considerations, it might affect their willingness to enter into such agreements."

I understand that such notions may give your negotiating team second thoughts. Playing hardball in a situation where public health is at stake is not easy.

But while you may be worried that Sanofi could walk away if pressed too hard on pricing, consider that the company also has something to lose — it would be turning its back on a potentially money-making vaccine that can be sold in numerous markets around the world.

In an era of rising drug costs — an issue that your boss has insisted must be solved — you have an opportunity to ensure that tax dollars spent subsidizing research provide a return on investment that benefits all Americans.

Questions from Ed Silverman at STAT:

Why is an exclusive license going to be granted?

And will the terms be disclosed?

NIAID Response (attributed generally to NIAID):

b5

From: Mowatt, Michael (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CB1EF7E2E54B4164AE34814574BDA638-MMOWATT]
Sent: 11/3/2017 6:51:05 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: Proposed grant of an exclusive license to Zika Vaccine

Understood.

We will draft a response and circulate.

b5

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, November 3, 2017 11:20 AM
To: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Subject: FW: Proposed grant of an exclusive license to Zika Vaccine

b5

From: Petrik, Amy (NIH/NIAID) [E]
Sent: Friday, November 03, 2017 10:52 AM
To: Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Cc: Salata, Carol (NIH/NIAID) [E] <csalata@niaid.nih.gov>; Feliccia, Vincent (NIH/NIAID) [E] <vfeliccia@niaid.nih.gov>; Green, Wade (NIH/NIAID) [E] <wade.green@nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>
Subject: RE: Proposed grant of an exclusive license to Zika Vaccine

Hi all,

I mistakenly added Natalie Greco instead of Wade Green so I'm adding Wade now.

Please use the recipients on this message for any new responses.

Thanks,
Amy

From: Stover, Kathy (NIH/NIAID) [E]
Sent: Friday, November 3, 2017 10:35 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Petrik, Amy (NIH/NIAID) [E] <amy.petrik@nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Cc: Salata, Carol (NIH/NIAID) [E] <csalata@niaid.nih.gov>; Feliccia, Vincent (NIH/NIAID) [E] <vfeliccia@niaid.nih.gov>; Greco, Natalie (NIH/NIAID) [C] <natalie.greco@nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>
Subject: RE: Proposed grant of an exclusive license to Zika Vaccine

Hi all,

In talking it over here at NIAID OCGR, we think

b5

b5

Best,

REL0000024325

Kathy

Kathy Stover
Branch Chief
News and Science Writing Branch
National Institute of Allergy and Infectious Diseases (NIAID)
Office of Communications and Government Relations
National Institutes of Health/HHS
31 Center Drive, Room 7A17E
Bethesda, MD 20892
Phone: (301) 496-8864
E-mail: kstover@nih.gov
NIAID Media Line: (301) 402-1663

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, November 03, 2017 9:59 AM
To: Petrik, Amy (NIH/NIAID) [E] <amy.petrik@nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Cc: Salata, Carol (NIH/NIAID) [E] <csalata@niaid.nih.gov>; Feliccia, Vincent (NIH/NIAID) [E] <vfeliccia@niaid.nih.gov>; Greco, Natalie (NIH/NIAID) [C] <natalie.greco@nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>; Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>
Subject: RE: Proposed grant of an exclusive license to Zika Vaccine

b5

From: Petrik, Amy (NIH/NIAID) [E]
Sent: Friday, November 03, 2017 8:31 AM
To: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Cc: Salata, Carol (NIH/NIAID) [E] <csalata@niaid.nih.gov>; Feliccia, Vincent (NIH/NIAID) [E] <vfeliccia@niaid.nih.gov>; Greco, Natalie (NIH/NIAID) [C] <natalie.greco@nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>; Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: FW: Proposed grant of an exclusive license to Zika Vaccine

Hi Mike,

Below is the message from KEI.

Thanks,
Amy

From: Kim Treanor [<mailto:kim.treanor@keionline.org>]
Sent: Wednesday, October 25, 2017 2:53 PM
To: Petrik, Amy (NIH/NIAID) [E] <amy.petrik@nih.gov>
Subject: Proposed grant of an exclusive license to Zika Vaccine

Dear Dr. Petrik,

I am writing in regards to the proposed grant of an exclusive patent license of a DNA-based vaccine for prevention of Zika virus infection to PaxVax Inc, as referenced in 82 FR 47537. As a part of this licensing agreement or separately from

REL0000024325

it, if the exclusive license is granted, will the NIAID or another division of the NIH also provide PaxVax with grants or financial support to conduct clinical trials on this vaccine candidate? PaxVax reports on their website that they have a Zika vaccine candidate in the pipeline which they are working on with the CDC. Do you know if this vaccine candidate has received any financial support from NIAID or another division of the NIH?

Thank you for your assistance.

Best regards,
Kim

--

Kim Treanor
Knowledge Ecology International
kim.treanor@keionline.org
tel.: +1.202.332.2670

From: Wong, Jennifer (NIH/NIMH) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=C4258C7CF58F4945A3DF079942C68852-WONGJE]
Sent: 5/28/2019 3:02:05 PM
To: Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Thank you!

From: Berkley, Dale (NIH/OD) [E]
Sent: Tuesday, May 28, 2019 10:34 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Sorry for the delay, good work Jennifer and great comments from Mark-

b5

b5 for your consideration in the attached.

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Friday, May 24, 2019 4:23 PM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, May 24, 2019 4:23 PM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Thanks Jenny. Looks good. I made a few proposed edits. Dale?

From: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Sent: Friday, May 24, 2019 3:47 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Hi all,

Attached is a draft response -- please feel free to modify.

b5

b5

Many thanks,
Jenny

REL0000024328

Jennifer Wong, M.S.
Technology Development Coordinator
National Institute of Mental Health
Office of Technology Transfer
35A Convent Drive, Room GE400
Bethesda, MD 20892-3747
Phone: 301-480-4821
E-mail: wongje@mail.nih.gov

Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, dissemination, distribution, copying, use of this email or information enclosed therein is strictly prohibited. If you have received this email in error, please notify the sender and destroy the message and any attachments without making a copy. Thank you.

From: Wong, Jennifer (NIH/NIMH) [E]
Sent: Wednesday, May 22, 2019 12:53 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Great! I'll send out a meeting invite with a call-in number.

Thanks,
Jenny

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, May 22, 2019 10:55 AM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Me too

From: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Sent: Wednesday, May 22, 2019 10:54 AM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Good for me

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Sent: Wednesday, May 22, 2019 10:52 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Hi,

How about 1:30 pm?

REL0000024328

Thanks,
Jenny

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, May 21, 2019 5:07 PM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

I can do Friday after 1

From: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Sent: Tuesday, May 21, 2019 4:50 PM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Oh I see that I'll be in route to downtown at that time. You guys go ahead without me, or I could join any time Friday.

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Sent: Tuesday, May 21, 2019 2:26 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Hi Mark,

Thursday between 2-4 pm is good. Please let me know when it would be convenient to chat. b5
b5 when KEI sent the
additional comments.

Thanks,
Jenny

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, May 21, 2019 11:29 AM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Cc: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

b5

Dale will join us if he is available to talk. Would Thursday after 2 work?

From: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Sent: Tuesday, May 21, 2019 9:15 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: FW: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

REL0000024328

Hi Mark,

Are you available to discuss?

Thanks,
Jenny

Jennifer Wong, M.S.
Technology Development Coordinator
National Institute of Mental Health
Office of Technology Transfer
35A Convent Drive, Room GE400
Bethesda, MD 20892-3747
Phone: 301-480-4821
E-mail: wongje@mail.nih.gov

Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, dissemination, distribution, copying, use of this email or information enclosed therein is strictly prohibited. If you have received this email in error, please notify the sender and destroy the message and any attachments without making a copy. Thank you.

From: Luis Gil Abinader <luis.gil.abinader@keionline.org>
Sent: Monday, May 20, 2019 4:51 PM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Cc: claire.cassedy <claire.cassedy@keionline.org>; Jamie Love <james.love@keionline.org>
Subject: 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Dear Jennifer Wong, MS,

Attached please find the comments by KEI and James Love as an individual with regards to the license proposed in the Federal Register notice 84 FR 19090 to Repurposed Therapeutics, Inc.

Best regards,

Luis Gil Abinader

From: Richard Gold, Prof. [richard.gold2@mcgill.ca]
Sent: 12/8/2017 8:00:51 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Tania Bubela [tbubela@ualberta.ca]; holmancm@umkc.edu
Subject: Re: balanced view on use of B-D march-in

Dear Mark,

Good to hear from you. I would think that Bob Cook-Deegan or Arti Rai could speak to this. Jake Sherkow may also be good but I do not know whether he has engaged in the issue of march-in rights.

Best,
Richard

From: "Rohrbaugh, Mark (NIH/OD) [E]" <rohrbaum@od.nih.gov>
Date: Thursday, December 7, 2017 at 11:28 AM
To: Tania Bubela <tbubela@ualberta.ca>, Richard Gold <richard.gold2@mcgill.ca>, "holmancm@umkc.edu" <holmancm@umkc.edu>
Subject: balanced view on use of B-D march-in

Tania, Richard and Chris:

I hope all is well with you. Recent news articles about march-in have focused primarily on the opinion and quotes from KEI. Do you know anyone who has written or might write, or speak to the press if asked, with a more balanced view of the march-in statute? Probably would be better if the person was US based.

Have a wonderful holiday and a healthy, productive 2019

Mark

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director
National Institutes of Health

From: Kassilke, Deborah (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=KASSILKE]
Sent: 1/18/2017 10:10:04 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Thomas, Gina (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=gthomas]
Subject: FW: KEI Request for CRADAs
Attachments: KEI FOIA 20150429.xlsx

Gina – please advise – do we have the actual information that was submitted to KEI for this foia request back in 2015? It looks like we DID provide a list of CRADAS. See below:

From: Thomas, Gina (NIH/OD) [E]
Sent: Wednesday, January 18, 2017 4:51 PM
To: Rogers, Karen (NIH/OD) [E] <RogersK@od.nih.gov>
Subject: FW: KEI Request for CRADAs

From: Goldstein, Bruce (NIH/OD) [E]
Sent: Tuesday, April 28, 2015 6:27 PM
To: Cornell, Susan (NIH/OD) [E] <CornellS@OD.NIH.GOV>
Cc: Ferguson, Steve (NIH/OD) [E] <FERGUSOS@od6100m1.od.nih.gov>; Thomas, Gina (NIH/OD) [E] <gthomas@od.nih.gov>
Subject: RE: KEI Request for CRADAs

Hi.

Tedious but very easy. I took the liberty of adding the current status of each CRADA, which might be helpful in narrowing their requests. I wasn't sure whether [REDACTED] b5

[REDACTED] b5

Regards,
Bruce D. Goldstein, Esq.
NIH Office of Technology Transfer

From: Thomas, Gina (NIH/OD) [E]
Sent: Tuesday, April 28, 2015 4:59 PM
To: Goldstein, Bruce (NIH/OD) [E]
Cc: Ferguson, Steve (NIH/OD) [E]
Subject: FW: KEI Request for CRADAs

Bruce can you please rerun the CRADA report with the items highlighted in yellow only.

[REDACTED] b5

Thanks

Gina

From: Cornell, Susan (NIH/OD) [E]
Sent: Tuesday, April 28, 2015 3:19 PM
To: Thomas, Gina (NIH/OD) [E]
Cc: Ferguson, Steve (NIH/OD) [E]; Berkley, Dale (NIH/OD) [E]
Subject: KEI Request for CRADAs

REL0000024330

Good Afternoon,

I just got off the phone with Ms. Cassidy of KEI. I explained that NIH has approximately 800 CRADAS and 500 amendments that fall within her timeframe and that our very conservative estimate of a total page count was 45,000 - 50,000 pages (many thanks, Gina, for those numbers!). She said they had no idea there would be that many. I suggested that she take a list of the CRADAs with the CRADA partner, the title and the date signed/executed and she said that would be great. **b5** FYI, that is the same information we provided to Public Citizen 15 years ago.

So, the question is this -

b5

b5

Thanks for your ongoing help with this one!

Susan

Susan R. Cornell, J.D.
Freedom of Information Officer
National Institutes of Health
Building 31, Room 5B35
9000 Rockville Pike
Bethesda, MD 20892

PH: 301-496-5633
FAX: 301-402-4541
EMAIL: cornells@od.nih.gov



REL0000024330

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 5/9/2018 8:34:29 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: Prospective Grant of Exclusive Patent License: Antibodies Against TL1A, a TNF-Family Cytokine, for the Treatment and Diagnosis of Crohn's Disease, Ulcerative Colitis, Asthma, Psoriasis and Biliary Cirrhosis

b5

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, May 09, 2018 4:26 PM
To: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: RE: Prospective Grant of Exclusive Patent License: Antibodies Against TL1A, a TNF-Family Cytokine, for the Treatment and Diagnosis of Crohn's Disease, Ulcerative Colitis, Asthma, Psoriasis and Biliary Cirrhosis

b5

From: Berkley, Dale (NIH/OD) [E]
Sent: Wednesday, May 09, 2018 4:24 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: Prospective Grant of Exclusive Patent License: Antibodies Against TL1A, a TNF-Family Cytokine, for the Treatment and Diagnosis of Crohn's Disease, Ulcerative Colitis, Asthma, Psoriasis and Biliary Cirrhosis

b5

Best, Dale

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, May 09, 2018 4:17 PM
To: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: FW: Prospective Grant of Exclusive Patent License: Antibodies Against TL1A, a TNF-Family Cytokine, for the Treatment and Diagnosis of Crohn's Disease, Ulcerative Colitis, Asthma, Psoriasis and Biliary Cirrhosis

b5

From: Shmilovich, Michael (NIH/NHLBI) [E]
Sent: Wednesday, May 09, 2018 12:44 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: FW: Prospective Grant of Exclusive Patent License: Antibodies Against TL1A, a TNF-Family Cytokine, for the Treatment and Diagnosis of Crohn's Disease, Ulcerative Colitis, Asthma, Psoriasis and Biliary Cirrhosis

REL0000024331

Enclosed. Dale's advice

b5

From: James Love <james.love@keionline.org>

Sent: Tuesday, May 08, 2018 16:25

To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>

Cc: manon.ress@keionline.org; claire.cassedy@keionline.org; Thalhammer-Reyero, Cristina (NIH/NHLBI) [E] <cristina.thalhammer-reyero@nih.gov>

Subject: Re: Prospective Grant of Exclusive Patent License: Antibodies Against TL1A, a TNF-Family Cytokine, for the Treatment and Diagnosis of Crohn's Disease, Ulcerative Colitis, Asthma, Psoriasis and Biliary Cirrhosis

Thank you, but with all due respect, the notice is something required by statute, to give the public a right to comment on a proposed license, and the federal register notice does not explain much about the terms of the license. So what exactly are we commenting on? Should the NIH grant a monopoly to this company on the technology, on any random terms? Why can't the NIH give the public more information about the proposed terms of the license? It does make a difference to us whether the exclusive rights are for the life of the patent or a shorter period, and if the license recognizes the importance of access in developing countries. And, we continue to express concern that the NIH is not addressing the statutory obligation to ensure that inventions are "available to the public on reasonable terms". If there are no restrictions on pricing, the case for a life of patent license is even weaker.

Jamie

On Tue, May 8, 2018 at 4:05 PM, Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov> wrote:

Dear Mr. Love:

Thank you for your email. Cristina will be out of the country until mid-June and will be unable to respond to your email directly.

With respect to your inquiry, we think that the Federal Register Notice adequately describes the nature of the intellectual property and our intentions regarding the proposed license. The purpose of the Notice was to solicit objections based on the information provided therein. If you have any such objections, please provide them to us before the deadline.

Sincerely,

Michael A. Shmilovich, Esq., CLP



National Heart, Lung,
and Blood Institute

Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479

REL0000024331

Bethesda, MD 20892-2479
o. 301.435.5019

shmilovm@mail.nih.gov

This message may contain privileged and confidential information intended only for the use of the individual(s) or entity named above. If you are not the intended recipient, you are hereby notified that any use, dissemination, distribution, or copying of this message or its content is strictly prohibited. If you have received this message in error, please notify sender immediately and destroy the message without making a copy. Thank you.

"Always be yourself...unless you can be a pyrate... then; obviously, be a pyrate"

From: James Love <james.love@keionline.org>

Sent: Monday, May 07, 2018 5:10 PM

To: Thalhammer-Reyero, Cristina (NIH/NHLBI) [E] <cristina.thalhammer-reyero@nih.gov>

Cc: Claire Cassedy <claire.cassedy@keionline.org>; Manon Ress <manon.ress@keionline.org>; Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>

Subject: Re: Prospective Grant of Exclusive Patent License: Antibodies Against TL1A, a TNF-Family Cytokine, for the Treatment and Diagnosis of Crohn's Disease, Ulcerative Colitis, Asthma, Psoriasis and Biliary Cirrhosis

Dear Dr. Thalhammer-Reyero,

Thank you. But for the comment on the proposed licence to be useful, we need more information than what was written in the Federal Register Notice. And that is why we are requesting additional information. Can you tell me if you intend to respond to any of the eight questions I asked?

Jamie

On Mon, May 7, 2018 at 5:00 PM, Thalhammer-Reyero, Cristina (NIH/NHLBI) [E] <cristina.thalhammer-reyero@nih.gov> wrote:

Dear Mr. Love,

REL0000024331

We welcome your comments regarding the FR notice.

Best regards,

Cristina Thalhammer-Reyero, Ph.D., M.B.A.

Senior Licensing and Patenting Manager

Office of Technology Transfer and Development

National Heart, Lung and Blood Institute

tel: : +1-301-435-4507

ThalhamC@mail.nih.gov

This message may contain privileged and confidential information intended only for the use of the individual(s) or entity named above. If you are not the intended recipient, you are hereby notified that any use, dissemination, distribution, or copying of this message or its content is strictly prohibited. If you have received this message in error, please notify sender immediately and destroy the message without making a copy. Thank you.

From: James Love <james.love@keionline.org>

Sent: Saturday, May 05, 2018 1:48 PM

To: Thalhammer-Reyero, Cristina (NIH/NHLBI) [E] <cristina.thalhammer-reyero@nih.gov>

Cc: Claire Cassedy <claire.cassedy@keionline.org>; Manon Ress <manon.ress@keionline.org>

Subject: Prospective Grant of Exclusive Patent License: Antibodies Against TL1A, a TNF-Family Cytokine, for the Treatment and Diagnosis of Crohn's Disease, Ulcerative Colitis, Asthma, Psoriasis and Biliary Cirrhosis

Cristina Thalhammer-Reyero, Ph.D., MBA,

Senior Licensing and Patenting Manager,

NHLBI Office of Technology Transfer and Development,

31 Center Drive Room 4A29, MSC2479, Bethesda, MD 20892-2479;

Telephone: +1-301-435-4507;

REL0000024331

Email: thalhamc@mail.nih.gov.

Dear Dr. Thalhammer-Reyero,

I plan to comment on the proposed license recently notices in the federal register, here: 83 FR 20081

I would like to know:

1. What is the proposed consideration for the license, including but not limited to the royalty rates?
2. What is the term of the license?
3. Has the NIH determined that a life of patent license is necessary, pursuant to 35 USC 209?
4. If yes to 3., what methodology was used?
5. Has the NIH determined that a worldwide license is necessary, pursuant to 35 USC 209?
6. What provisions does the NIH propose to ensure the inventions are "available to the public on reasonable terms"?
7. What measures has the NIH taken to ensure the inventions will be accessible to persons living in developing countries?
8. Has the NIH obtained the advice of the Attorney General, pursuant to 40 USC 559?

James Love

--

James Love. Knowledge Ecology International
<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584,
twitter.com/jamie_love

--

James Love. Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

From: Mowatt, Michael (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CB1EF7E2E54B4164AE34814574BDA638-MMOWATT]
Sent: 11/6/2017 9:57:24 PM
To: Stover, Kathy (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c82722674ba14c2f969bd50dfa6a7af4-stoverk]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Salata, Carol (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f98ca6a1f9fc4cfdbbf4036ca8cbace4-csalata]; Feliccia, Vincent (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7f3a54860cb941c1abe1df786e478e00-vfeliccia]; Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]; Mowatt, Michael (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb1ef7e2e54b4164ae34814574bda638-mmowatt]; Petrik, Amy (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c4ec05a179f04067b61f20605e911e7c-petrika]
Subject: RE: Proposed grant of an exclusive license to Zika Vaccine
Attachments: Response to KTreanor DRAFT 171106.docx

See proposed draft (attached).

From: Stover, Kathy (NIH/NIAID) [E]
Sent: Friday, November 3, 2017 10:35 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Petrik, Amy (NIH/NIAID) [E] <amy.petrik@nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Cc: Salata, Carol (NIH/NIAID) [E] <csalata@niaid.nih.gov>; Feliccia, Vincent (NIH/NIAID) [E] <vfeliccia@niaid.nih.gov>; Greco, Natalie (NIH/NIAID) [C] <natalie.greco@nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>
Subject: RE: Proposed grant of an exclusive license to Zika Vaccine

Hi all,

In talking it over here at NIAID OCGR, we think

b5

b5

Best,
Kathy

Kathy Stover
Branch Chief
News and Science Writing Branch
National Institute of Allergy and Infectious Diseases (NIAID)
Office of Communications and Government Relations
National Institutes of Health/HHS
31 Center Drive, Room 7A17E
Bethesda, MD 20892
Phone: (301) 496-8864
E-mail: kstover@nih.gov
NIAID Media Line: (301) 402-1663

REL0000024336

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, November 03, 2017 9:59 AM
To: Petrik, Amy (NIH/NIAID) [E] <amy.petrik@nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Cc: Salata, Carol (NIH/NIAID) [E] <csalata@niaid.nih.gov>; Feliccia, Vincent (NIH/NIAID) [E] <vfeliccia@niaid.nih.gov>; Greco, Natalie (NIH/NIAID) [C] <natalie.greco@nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>; Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>
Subject: RE: Proposed grant of an exclusive license to Zika Vaccine

b5

From: Petrik, Amy (NIH/NIAID) [E]
Sent: Friday, November 03, 2017 8:31 AM
To: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Cc: Salata, Carol (NIH/NIAID) [E] <csalata@niaid.nih.gov>; Feliccia, Vincent (NIH/NIAID) [E] <vfeliccia@niaid.nih.gov>; Greco, Natalie (NIH/NIAID) [C] <natalie.greco@nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>; Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: FW: Proposed grant of an exclusive license to Zika Vaccine

Hi Mike,

Below is the message from KEI.

Thanks,
Amy

From: Kim Treanor [<mailto:kim.treanor@keionline.org>]
Sent: Wednesday, October 25, 2017 2:53 PM
To: Petrik, Amy (NIH/NIAID) [E] <amy.petrik@nih.gov>
Subject: Proposed grant of an exclusive license to Zika Vaccine

Dear Dr. Petrik,

I am writing in regards to the proposed grant of an exclusive patent license of a DNA-based vaccine for prevention of Zika virus infection to PaxVax Inc, as referenced in 82 FR 47537. As a part of this licensing agreement or separately from it, if the exclusive license is granted, will the NIAID or another division of the NIH also provide PaxVax with grants or financial support to conduct clinical trials on this vaccine candidate? PaxVax reports on their website that they have a Zika vaccine candidate in the pipeline which they are working on with the CDC. Do you know if this vaccine candidate has received any financial support from NIAID or another division of the NIH?

Thank you for your assistance.

Best regards,
Kim

--

Kim Treanor

REL0000024336

Knowledge Ecology International
kim.treanor@keionline.org
tel.: +1.202.332.2670

b5

b5

From: Predescu, Alina (NIH/NCATS) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=1A60E98376E746C7A37640BD40F45149-PREDESCUAD]
Sent: 5/25/2019 3:15:47 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: IP Watchdog blog about march-in and KEI

Hi Mark,

b6

Have a great holiday weekend,
Alina

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Thursday, May 23, 2019 6:57 PM
To: Predescu, Alina (NIH/NCATS) [E] <alina.predescu@nih.gov>
Subject: RE: IP Watchdog blog about march-in and KEI

Hi Alina. b6 Thanks much.

From: Predescu, Alina (NIH/NCATS) [E] <alina.predescu@nih.gov>
Sent: Thursday, May 23, 2019 11:20 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: IP Watchdog blog about march-in and KEI

Hi Mark,

I am following up on our conversation as well as the conversation I had with Carrie Wolinetz. b6

b6

Thank you and have a wonderful holiday weekend,

Alina

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Tuesday, May 14, 2019 12:02 PM
To: Predescu, Alina (NIH/NCATS) [E] <alina.predescu@nih.gov>
Subject: RE: IP Watchdog blog about march-in and KEI

I had a conflict and could not attend. Tom will fill me in later.

From: Predescu, Alina (NIH/NCATS) [E] <alina.predescu@nih.gov>
Sent: Tuesday, May 14, 2019 11:21 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: IP Watchdog blog about march-in and KEI

Hi Mark,

REL0000024337

Thank you for sharing this.

I just had a call with Carrie Wolinetz and we had a great conversation. I look forward to hear the next steps.

Also, will you be able to join the meeting with Tom Stackhouse on the NIH TT Publications?

Best,
Alina

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, May 13, 2019 5:21 PM
To: NIH TDC Long <niaaatdcl-l@mail.nih.gov>
Subject: IP Watchdog blog about march-in and KEI

<https://www.ipwatchdog.com/2019/05/12/knowledge-ecology-international-letter-misleads-march-rights/id=109152/>

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Office of Science Policy
National Institutes of Health

From: Holman, Christopher M. [holmancm@umkc.edu]
Sent: 12/8/2017 3:55:35 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: balanced view on use of B-D march-in

Hi Mark,

I would not mind speaking to someone from press, [b4,b6] but have not given it much thought recently. Don't know of any better candidate off hand. Hope all is well with you.

Best regards,

Chris

Chris Holman
Professor of Law
UMKC School of Law
5100 Rockhill Road
Kansas City, MO 64110
816.235.2384
holmancm@umkc.edu

I use voice recognition software, which at times lead to bizarre typographical errors, for which I apologize.

You can access my papers on the Social Science Research Network (SSRN) at: <http://ssrn.com/author=537838>

From: Rohrbaugh, Mark (NIH/OD) [E] [mailto:rohrbaum@od.nih.gov]
Sent: Thursday, December 07, 2017 10:28 AM
To: Tania Bubela <tbubela@ualberta.ca>; richard.gold2@mcgill.ca; Holman, Christopher M. <holmancm@umkc.edu>
Subject: balanced view on use of B-D march-in

Tania, Richard and Chris:

I hope all is well with you. Recent news articles about march-in have focused primarily on the opinion and quotes from KEI. Do you know anyone who has written or might write, or speak to the press if asked, with a more balanced view of the march-in statute? Probably would be better if the person was US based.

Have a wonderful holiday and a healthy, productive 2019

Mark

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director

REL0000024338

From: Kassilke, Deborah (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=KASSILKE]
Sent: 1/18/2017 9:12:36 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: FOIA list of CRADAs
Attachments: FW: New FOIA Request - Royalty Payments

b5

b5

I'll check with Karen R.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, January 18, 2017 4:10 PM
To: Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov>
Subject: RE: FOIA list of CRADAs

b5

From: Kassilke, Deborah (NIH/OD) [E]
Sent: Wednesday, January 18, 2017 4:05 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: FOIA list of CRADAs

b5

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, January 18, 2017 4:03 PM
To: Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov>
Subject: RE: FOIA list of CRADAs

b5

From: Kassilke, Deborah (NIH/OD) [E]
Sent: Wednesday, January 18, 2017 4:01 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: FOIA list of CRADAs

I'm still struggling with FOIA – it is one area I just don't have much experience with. Susan Cornell is missed.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, January 18, 2017 3:22 PM
To: Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov>
Subject: RE: FOIA list of CRADAs

b5

From: Kassilke, Deborah (NIH/OD) [E]
Sent: Wednesday, January 18, 2017 3:06 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: FOIA list of CRADAs

Hmmm – help me with

b5

b5

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, January 18, 2017 2:59 PM
To: Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov>
Subject: RE: FOIA list of CRADAs

In thinking about Ann's comment

b5

b5

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, January 18, 2017 2:30 PM
To: Kassilke, Deborah (NIH/OD) [E] <deborah.kassilke@nih.gov>
Subject: FW: FOIA list of CRADAs

Ann's take on it.

From: Hammersla, Ann (NIH/OD) [E]
Sent: Wednesday, January 18, 2017 2:28 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: FOIA list of CRADAs

Depends:

b5

Ann

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, January 18, 2017 2:19 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: FOIA list of CRADAs

Ann:

Deb asked me and I thought you might have insights.

b5

but wanted your opinion.

b5

Thanks

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director
National Institutes of Health

From: Cornell, Susan (NIH/OD) [E] [/O=NIH/OU=NIH/OD/CN=OD/CN=CORNELLS]
Sent: 8/15/2016 9:21:46 PM
To: Kassilke, Deborah (NIH/OD) [E] [/O=NIH/OU=NIH/OD/CN=OD/CN=KASSILKE]; Rogers, Karen (NIH/OD) [E] [/O=NIH/OU=NIH/OD/CN=OD/CN=ROGERS]
CC: Collins, Deborah (NIH/OD) [E] [/O=NIH/OU=NIH/OD/CN=OD/CN=COLLINS]
Subject: FW: New FOIA Request - Royalty Payments

Deb and Karen –

FYI.

Debbie – Since Karen is out can we chat about how to approach this one? I've got lots of questions but not many answers!

Thanks,

Susan



From: Cornell, Susan (NIH/OD) [E]
Sent: Monday, August 15, 2016 5:14 PM
To: Burklow, John (NIH/OD) [E] <BurklowJ@OD.NIH.GOV>; Allen, Marin (NIH/OD) [E] <AllenM1@mail.nih.gov>; Jackson, Calvin (NIH/OD) [E] <JACKSONC@od31tm1.od.nih.gov>
Subject: New FOIA Request - Royalty Payments

Hi – We've received a request from Knowledge Ecology International seeking information on royalty payments paid to individual employees, specifically:

1. All records related to individual royalty payments for licensed technologies received by every current or former federal employee for whom NIH administers royalty payments including NIH, CDC, and FDA employees;

And

2. All communications and correspondence to or from employees of NIH, CDC, and FDA that mention the payment of such royalties to current or former individual employees of NIH, CDC and FDA.

The timeframe of the request is August 8, 2011 and August 8, 2016.

Susan

Susan R. Cornell, J.D.
Freedom of Information Officer
National Institutes of Health
Building 31, Room 5B35
9000 Rockville Pike
Bethesda, MD 20892

REL0000024340.0001

PH: 301-496-5633
FAX: 301-402-4541
EMAIL: cornells@od.nih.gov



From: Wong, Jennifer (NIH/NIMH) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=C4258C7CF58F4945A3DF079942C68852-WONGJE]
Sent: 5/24/2019 7:47:07 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics
Attachments: Response to FR notice comments from KEI.docx; Scopolamine Publication.pdf

Hi all,

Attached is a draft response -- please feel free to modify as well.

b5

Many thanks,
Jenny

Jennifer Wong, M.S.
Technology Development Coordinator
National Institute of Mental Health
Office of Technology Transfer
35A Convent Drive, Room GE400
Bethesda, MD 20892-3747
Phone: 301-480-4821
E-mail: wongje@mail.nih.gov

Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, dissemination, distribution, copying, use of this email or information enclosed therein is strictly prohibited. If you have received this email in error, please notify the sender and destroy the message and any attachments without making a copy. Thank you.

From: Wong, Jennifer (NIH/NIMH) [E]
Sent: Wednesday, May 22, 2019 12:53 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Great! I'll send out a meeting invite with a call-in number.

Thanks,
Jenny

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, May 22, 2019 10:55 AM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Me too

From: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Sent: Wednesday, May 22, 2019 10:54 AM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

REL0000024347

Good for me

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Sent: Wednesday, May 22, 2019 10:52 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Hi,

How about 1:30 pm?

Thanks,
Jenny

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, May 21, 2019 5:07 PM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

I can do Friday after 1

From: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Sent: Tuesday, May 21, 2019 4:50 PM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Oh I see that I'll be in route to downtown at that time. You guys go ahead without me, or I could join any time Friday.

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Sent: Tuesday, May 21, 2019 2:26 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Hi Mark,

Thursday between 2-4 pm is good. Please let me know when it would be convenient to chat.

b5

b5

when KEI sent the additional comments.

REL0000024347

Thanks,
Jenny

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, May 21, 2019 11:29 AM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Cc: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

b5

Dale will join us if he is available to talk. Would Thursday after 2 work?

From: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Sent: Tuesday, May 21, 2019 9:15 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: FW: KEI-- 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Hi Mark,

Are you available to discuss?

Thanks,
Jenny

Jennifer Wong, M.S.
Technology Development Coordinator
National Institute of Mental Health
Office of Technology Transfer
35A Convent Drive, Room GE400
Bethesda, MD 20892-3747
Phone: 301-480-4821
E-mail: wongje@mail.nih.gov

Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, dissemination, distribution, copying, use of this email or information enclosed therein is strictly prohibited. If you have received this email in error, please notify the sender and destroy the message and any attachments without making a copy. Thank you.

From: Luis Gil Abinader <luis.gil.abinader@keionline.org>
Sent: Monday, May 20, 2019 4:51 PM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Cc: claire.cassedy <claire.cassedy@keionline.org>; Jamie Love <james.love@keionline.org>
Subject: 84 FR 19090, Prospective Grant of Exclusive Patent License: Scopolamine Therapeutics

Dear Jennifer Wong, MS,

Attached please find the comments by KEI and James Love as an individual with regards to the license proposed in the Federal Register notice 84 FR 19090 to Repurposed Therapeutics, Inc.

Best regards,

Luis Gil Abinader

REL0000024347

b5

REGULAR RESEARCH ARTICLE

Neurophysiological Changes Associated with Antidepressant Response to Ketamine Not Observed in a Negative Trial of Scopolamine in Major Depressive Disorder

Lawrence Park, Maura Furey, Allison C. Nugent, Cristan Farmer, Jessica Ellis, Joanna Szczepanik, Marc S. Lener, Carlos A. Zarate Jr.

Experimental Therapeutics and Pathophysiology Branch, Intramural Research Program, National Institute of Mental Health, National Institutes of Health, Bethesda, Maryland (Drs Park, Nugent, Farmer, Szczepanik, Lener, and Zarate); Janssen Research and Development, LLC, La Jolla, California (Dr Furey); Department of Psychiatry, University of Maryland School of Medicine, Baltimore, Maryland (Dr Ellis).

L.P. and M.F. contributed equally.

Correspondence: Lawrence Park, MD, 10 Center Drive, MSC 1282, Bldg, 10CRC, Rm. 7-3465, Bethesda, Maryland, 20892-1282 (Lawrence.park@nih.gov).

Abstract

Background: This randomized, placebo-controlled, crossover trial examined the antidepressant efficacy of the muscarinic antagonist scopolamine in major depressive disorder subjects with more severe and refractory forms of major depressive disorder relative to previous reports.

Methods: Participants included 23 medication-free major depressive disorder subjects (12 F/11 M, 20–55 years) currently experiencing a major depressive episode. Subjects had scored ≥ 20 on the Montgomery-Asberg Depression Rating Scale. Following a single-blind, placebo lead-in, participants were randomized to receive 2 counterbalanced blocks of 3 i.v. infusions of scopolamine (4 $\mu\text{g/kg}$) and placebo in a double-blind manner. The primary and secondary outcomes were the Montgomery-Asberg Depression Rating Scale and the Hamilton Anxiety Rating Scale, respectively. Magnetoencephalography and plasma brain-derived neurotrophic factor concentrations were obtained prior to and after each treatment phase.

Results: As assessed by both the Montgomery-Asberg Depression Rating Scale and Hamilton Anxiety Rating Scale, scopolamine had no significant antidepressant or anxiolytic effects relative to placebo. No significant drug vs placebo effects were seen in magnetoencephalography gamma power or brain-derived neurotrophic factor plasma concentrations, and brain-derived neurotrophic factor changes did not correlate with change in Montgomery-Asberg Depression Rating Scale score in response to scopolamine.

Conclusions: These results do not support the efficacy of scopolamine for more severe or refractory forms of depression. No pre- to post-infusion changes in plasma brain-derived neurotrophic factor were detected, and magnetoencephalography gamma power changed only in the placebo lead-in, suggesting that these biomarker measures were not affected by scopolamine in this cohort. While difficult to interpret given the lack of antidepressant response, the findings suggest that the neurobiological effects of ketamine and scopolamine are at least partly distinct.

Keywords: scopolamine, major depressive disorder, ketamine, biomarkers

Received: March 3, 2018; Revised: May 9, 2018; Accepted: July 27, 2018

Published by Oxford University Press on behalf of CINP 2018. This work is written by (a) US Government employee(s) and is in the public domain in the US.

This Open Access article contains public sector information licensed under the Open Government Licence v2.0 (<http://www.nationalarchives.gov.uk/doc/open-government-licence/version/2/>).

Significance Statement

In this crossover trial of subjects with major depressive disorder (MDD), scopolamine administration was not associated with significant improvement in depressive or anxious symptoms compared to placebo. Subjects in this trial may have been more treatment-resistant than in previous scopolamine studies. Neurophysiological markers such as magnetoencephalography (MEG) gamma power and plasma brain derived neurotrophic factor (BDNF) levels—which have been shown to change in response to ketamine administration—demonstrated no significant association with scopolamine administration. These findings do not provide evidence that scopolamine and ketamine exert similar neurobiological effects.

Introduction

Major depressive disorder (MDD) is a major public health concern. Almost one-third of individuals in the US will experience a major depressive episode at some point in their lives (Kessler et al., 2012). Of those who screen positive for depression, more than 70% will not receive appropriate treatment (Olfson et al., 2016), perhaps discouraged by the significant lag time between starting medications and symptomatic relief or by the relative lack of efficacy of current treatment options. For instance, up to one-third of MDD subjects will not achieve symptom remission even after 4 antidepressant trials (Trivedi et al., 2006a, 2006b). Psychopharmacological research over the past few decades has not significantly advanced the number of approved drug treatments for depression beyond the monoaminergic interventions in use for more than 50 years. Thus, the need to develop new and rapid antidepressant treatments is great and will likely require targeting novel neurobiological substrates.

The cholinergic neurotransmitter system, both muscarinic and nicotinic receptors, has been implicated as a potential substrate of rapid antidepressant response. The muscarinic cholinergic system in particular has considerable preclinical and clinical evidence to support its role in regulating mood symptoms (Drevets et al., 2013). Several decades ago, Janowsky and colleagues hypothesized that an adrenergic/cholinergic balance underlies mood disorders (Janowsky et al., 1972). In preclinical studies, rats bred selectively for supersensitivity of the muscarinic receptors (the Flinders Sensitive Line) displayed behavioral depressive-like symptoms in the presence of agents that increase cholinergic function, including increased behavioral despair in the forced swim test (Overstreet et al., 1992). Anticholinergic agents such as scopolamine were found to reduce behavioral despair in animals (Betin et al., 1982). In humans, challenge studies found that the anticholinesterase inhibitor physostigmine increased cholinergic activity and exacerbated depressive symptoms in currently depressed MDD subjects (Janowsky et al., 1972, 1974; Risch et al., 1981; Nurnberger et al., 1983). Physiologic studies found that neuroendocrine and pupillary responses to physostigmine were abnormally increased in depressed individuals (Janowsky et al., 1985; Dilsaver, 1986; Rubin et al., 1999), and genetic studies found that a variation in the type 2 muscarinic (M2) cholinergic receptor gene was associated with an elevated incidence or severity of MDD (Comings et al., 2002; Wang et al., 2004; Cannon et al., 2011).

In treatment trials, open-label administration of the muscarinic receptor antagonist scopolamine (0.4 mg i.m.) to 10 depressed patients and 10 healthy controls before bedtime for 3 consecutive nights was found to have a small but statistically significant antidepressant effect on the second morning of treatment (Gillin et al., 1991). Furey and Drevets, investigating the role of the cholinergic system in the cognitive symptoms of depression, unexpectedly found that scopolamine had rapid antidepressant effects in depressed subjects. In the first of the 2 studies (Furey and Drevets,

2006), 19 medication-free subjects meeting DSM-IV criteria for recurrent MDD or bipolar disorder (subjects were not required to be treatment resistant) were included in a double-blind, placebo-controlled pilot outpatient study; 6 subjects had been chronically ill (more than 2 years) and one was unresponsive to previous treatment. Scopolamine hydrobromide (4 µg/kg) administered i.v. over 15 minutes rapidly reduced the severity of depressive symptoms within 3 to 5 days after the first treatment (effect size 2.2–3.4), although subjects reported marked improvements in clinical symptoms by the evening or the morning after scopolamine administration. A subsequent study (Drevets and Furey, 2010) replicated this initial finding; scopolamine's antidepressant efficacy was observed within 3 to 5 days in 23 outpatients with MDD (effect size 1.2–1.7). Across both groups (i.e., placebo/active and active/placebo) of this second double-blind, placebo-controlled, crossover study, 13 of 22 subjects were chronically ill (more than 2 years duration), and 6 of 22 had not responded to treatment in a previous depressive episode (one subject dropped out prior to receiving any intervention).

Ketamine, a glutamatergic modulator with antagonistic properties at the N-methyl-D-aspartate receptor, has similarly demonstrated rapid, though short-lived, antidepressant effects (Kishimoto et al., 2016). In one study, effect sizes were 1.46 at day 1 and 0.68 at 1 week post-ketamine infusion (Zarate et al., 2006). Preclinical studies have found that ketamine and scopolamine produce comparable antidepressant effects, suggesting that the 2 agents may share common cellular and molecular mechanisms that rapidly increase extracellular glutamate. For instance, both drugs are thought to exert their effects on gamma-aminobutyric acid (GABA)-ergic interneurons that synapse on presynaptic glutamatergic neurons in the prefrontal cortex; ketamine blocks interneuron N-methyl-D-aspartate receptors and scopolamine blocks muscarinic receptors (Li et al., 2010; Voleti et al., 2013; Wohleb et al., 2017). These two initial actions inhibit the inhibitory interneuron, resulting in decreased GABAergic activity that, in turn, leads to disinhibition of pyramidal neurons and increased extracellular glutamate release, activation of the mammalian target of rapamycin complex 1 cascade, elevated brain derived neurotrophic factor (BDNF) concentrations, and an increased number and function of spine synapses in the prefrontal cortex (Li et al., 2010; Voleti et al., 2013; Hare et al., 2017; Wohleb et al., 2017).

We previously suggested that a novel approach to developing biomarkers of antidepressant response would be to contrast interventions with a rapid onset of action, such as sleep deprivation or i.v. drugs (e.g., ketamine or scopolamine) (Zarate et al., 2013; Niciu et al., 2014). Increases in plasma BDNF levels have been shown to be associated with antidepressant response to ketamine (Haile et al., 2014), though other studies have not demonstrated this association (Machado-Vieira et al., 2009). In animal models, BDNF release was recently shown to be necessary for scopolamine's

antidepressant effects (Ghosal et al., 2018). Neuroimaging modalities may also offer an important tool for assessing target engagement and understanding the underlying mechanisms of drug action (Carmichael et al., 2017). A recent study of subjects with treatment-resistant MDD who received i.v. ketamine found that depressed and healthy subjects exhibited robust increases in gamma power in response to ketamine administration (Nugent et al., 2018). The relationship between increased gamma power and antidepressant response was modulated by baseline gamma levels, such that large increases in gamma power were associated with better antidepressant response in MDD subjects with lower baseline gamma; this relationship was inverted in MDD subjects with higher baseline gamma.

This study sought to examine the antidepressant efficacy of the muscarinic antagonist scopolamine in MDD patients across a broad range of severity and treatment resistance (i.e., there were no exclusion criteria for symptom severity or past number of treatment trials). This study also sought to generate preliminary evidence for a shared mechanism of action between ketamine and scopolamine, testing the hypothesis that, like ketamine, scopolamine's antidepressant effects would be associated with increased plasma BDNF and increased MEG gamma power from baseline to post-treatment.

METHODS

Participants

Subjects were recruited from local inpatient psychiatric units, the internet, and local and national physician referrals and were studied as inpatients ($n = 7$) and outpatients ($n = 16$) at the National Institute of Mental Health (NIMH) Mood Disorders Research Unit in Bethesda, Maryland. Eligible participants were 11 male and 12 female inpatients, 18 to 55 years old ($n = 23$); all subjects were diagnosed with MDD, currently depressed without psychotic features, as assessed by the Structured Clinical Interview for Axis I DSM-IV Disorders—Patient Version (First et al., 2001), and were required to have a score ≥ 20 on the Montgomery-Asberg Depression Rating Scale (MADRS) at screening and at the start of each infusion.

Subjects were judged clinically not to be at serious risk for suicide. Other exclusion criteria included a history of drug or alcohol abuse within 1 year or a lifetime history of alcohol or

drug dependence; a current or past history of other Axis I disorders that preceded the onset of MDD; general MRI exclusion criteria; vision and/or hearing problems severe enough to interfere with testing; electrocardiographic evidence of ischemia, arrhythmia, conduction defect, or myocardial infarction; current blood pressure of >140 mm Hg or <90 mm Hg systolic, or >90 mm Hg diastolic; clinically significant cerebrovascular or cardiovascular disease; congestive heart disease; angina pectoris; advanced arteriosclerosis; gross neurological impairment; hyperthyroidism; known hypersensitivity to anticholinergic agents; renal or hepatic impairment; clinical history of glaucoma or narrow angle glaucoma; age of onset of MDD >45 years; exposure within 2 weeks to medications likely to affect cerebral blood flow and metabolism or likely to interact with anti-cholinergic medications (e.g., narcotics or anti-cholinergic agents), as verified by history and urine drug screen; concomitant treatment with psychotropic medications in the two weeks before randomization (6 weeks for fluoxetine); and weight >275 pounds. In addition, female subjects could not be pregnant or nursing.

All subjects were in good physical health, as determined by medical history, physical exam, blood labs, ECG, chest x-ray, urinalysis, and toxicology. The study was approved by the Combined Neuroscience Institutional Review Board at the National Institutes of Health (NIH; NCT00369915). All subjects provided written informed consent before entry into the study and were assigned a Clinical Research Advocate from the NIMH Human Subjects Protection Unit to monitor the consent process and research participation throughout the study.

Study Design

Based on prior studies, an effect size ($d = 0.8$) was used to estimate the difference between pre- and post-treatment response for the purposes of the power calculation. With 80% power to detect an effect using 2-tailed significance at 0.05, we estimated that a minimum of 15 subjects would be needed.

This was a single-center, randomized, placebo-controlled, crossover design with a single-blind placebo lead-in. After a 2-week drug-free period, seven 15-minute infusions of either placebo or 4 $\mu\text{g/kg}$ of scopolamine were administered (Figure 1). The first of these infusions was the single-blind placebo lead-in, followed by 2 blocks of 3 placebo or scopolamine infusions. Study participants were randomized to block order (placebo/

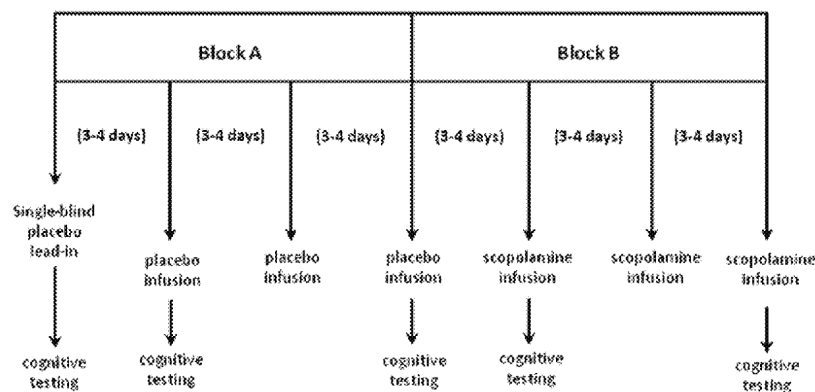


Figure 1. Study design. Following a 2-week wash-out and a single-blind placebo lead-in, participants were randomized to receive 2 counterbalanced blocks of 3 i.v. infusions of scopolamine (4 $\mu\text{g/kg}$) and placebo infusions. Block order was randomized and infusions were administered in a double-blind manner. Please note that the last follow-up visit is not represented in this diagram. Missing data: In placebo/scopolamine (P/S) group, Block 2, visit 2: $n = 2$ missing Montgomery-Asberg Depression Rating Scale (MADRS), $n = 4$ missing Hamilton Anxiety Rating Scale (HAM-A); in S/P group, Block 0, visits 1 and 2: $n = 1$ missing HAM-A, Block 1, visit 1: $n = 1$ missing HAM-A, Block 2, visit 2: $n = 2$ missing MADRS, $n = 4$ missing HAM-A.

scopolamine (P/S): $n = 11$; scopolamine/placebo (S/P): $n = 12$). Blocks were counterbalanced across subjects so that there were equal numbers of P/S and S/P block orders. Both the MADRS and the Hamilton Anxiety Rating Scale (HAM-A) were administered prior to each infusion and at the final follow-up visit.

Vital signs were monitored during the infusion and for 135 minutes post-infusion. An ECG, complete blood counts, electrolyte panels, and liver function tests were obtained at baseline and at the end of the study.

Data Collection

The primary outcome measure was the MADRS, a 10-item clinician-administered scale of depressive symptoms, and the secondary outcome was the HAM-A. Antidepressant response was defined using existing conventions to classify percent improvement from the final assessment of the placebo lead-in: improvements $\geq 50\%$ on the MADRS were considered full response and MADRS scores ≤ 10 indicated remission (Zimmerman et al., 2004). Although the number of prior treatment trial failures was not systematically collected, past treatment history was assessed through clinician interviews of medical and psychiatric history. The maximum number of failed prior antidepressant treatment trials was not an exclusion.

Resting-state MEG recordings were obtained following the single-blind placebo lead-in and on the day of the infusion (SCOP-Day0 and Placebo-Day0). Up to two 250-second resting state recordings per time point were analyzed; in general, one recording occurred at the beginning of the session, and the second was acquired approximately 30 minutes to 1 hour later after a series of tasks (to be reported elsewhere). For the resting state recordings, subjects were instructed to relax with their eyes closed and remain still. All data were acquired on a 275-channel CTF system at 1200 Hz. Background environmental magnetic noise was attenuated by synthetic third gradient balancing. T1 weighted MRI scans were acquired on a 3T GE scanner for co-registration.

Blood samples (for BDNF) were obtained using the vacutainer system prior to and after each treatment phase, as previously described (Machado-Vieira et al., 2009). Briefly, blood samples were centrifuged at 1000 rpm at 4°C for 5 minutes and stored at -80°C until assay. BDNF concentrations were measured using an anti-BDNF sandwich ELISA kit (Chemicon International) according to the manufacturer's instructions. Plasma was diluted 1:2 with sample buffer and carried out in duplicate blind to clinical information. BDNF standard solution was diluted to concentrations from 7.8 to 500 pg/mL of BDNF in a microplate reader to create the standard curve for BDNF concentrations. After the addition of streptavidin enzyme, substrate, and stop solution, BDNF concentrations were determined by absorbance in 450 nm using optical density values based on the standard curve values.

Statistical Analysis

Clinical Data Analysis

The model was a repeated-measures ANOVA with a compound symmetry covariance structure and restricted maximum likelihood estimation with a random effect of subject. Degrees of freedom were calculated using the Satterthwaite approximation. The first and last on-drug assessments for each period were selected for analysis, such that baseline assessments 1 and 2 formed Block 0, assessments 3 and 5 formed Block 1, and assessments 6 and 8 formed Block 2. The model included effects for randomization, block, assessment, and their interactions.

Significant interactions were probed using posthoc tests with Tukey-Kramer adjustment. Effect sizes were quantified using the least square mean estimates. Although mixed models are robust to missing data, which did occur in this study, the missing data at random assumption is not directly testable. For this reason, we carried out 2 sensitivity analyses to assess the robustness of the primary outcome. First, we excluded altogether participants for whom any datapoint was missing. Second, we analyzed the first arm of the trial as a parallel design. Complementary analyses were performed to analyze secondary hypotheses. In these mixed models, baseline values were controlled and fixed effects of block (Block 1 or Block 2), order (randomization group), assessment (first or last within block), and drug (scopolamine versus placebo) were entered. Again, the model was a repeated-measures ANOVA with a compound symmetry covariance structure and restricted maximum likelihood estimation, with a random effect of subject. All data analyses were performed using SAS/STAT Version 9.3.

MEG Data Analysis

MEG data were processed using CTF software (<http://www.ctf.com>), MNE-python (Gramfort et al., 2013), Analysis of Functional NeuroImages (AFNI) (Cox, 1996), and routines developed in-house. This work used the computational resources of the NIH HPC Biowulf cluster (<http://hpc.nih.gov>). Each MEG dataset was filtered using a high-pass filter of 2 Hz and visually inspected to identify and mark time periods with significant muscular, ocular, or movement artifacts. Up to 10 segments of 15-second duration outside marked artifacts were identified in an automated fashion. Datasets were discarded if at least five 15-second artifact-free segments could not be defined. All further described imaging analyses and quality control measures were carried out on the clean epochs.

Data were localized to source space on a 5-mm grid using synthetic aperture magnetometry (Robinson and Vrba, 1999), and a multisphere head model was calculated from co-registered MRI scans. MRI and MEG images were coregistered using MRI-visible fiducial markers placed on the head at the time of MRI scanning. Beamformer weights were calculated using a band-pass frequency of 2 to 100 Hz, and power was normalized by the projected noise floor of the virtual sensor. The resulting images represented root-mean-square power in the gamma band (30–50 Hz). All images were warped to Talairach space using AFNI and masked to remove non-brain matter and cerebellum. The final gamma band images were then normalized by the square root of the sum of squared images for 6 canonical bands between 2 and 100 Hz (delta, theta, alpha, beta, gamma, and high gamma). From this point forward, “gamma power” refers to the normalized root-mean-square gamma power.

Images were analyzed using a linear mixed model implemented in the AFNI routine 3dLME (Chen et al., 2013). If more than one usable recording existed for a given subject and session, both were included and coded as having occurred before or after a battery of cognitive tasks (to be reported elsewhere). MEG scans were obtained 60 to 120 minutes following scopolamine or placebo infusion. Session (baseline, Placebo-Day0, SCOP-Day0) and run number (first or second recording) were included in the model. The initial baseline scan was conducted during the placebo lead-in phase. Gender and age were initially included as main effects and removed if nonsignificant. Posthoc tests were performed within the 3dLME routine to assess individual contrasts. False discovery rate (FDR) over the contrast image was used to determine significance, with a threshold set at $P_{\text{FDR}} < .05$.

BDNF

Plasma BDNF concentrations were measured immediately before and 150 minutes after the first infusion of each condition (i.e., Session 2 and Session 5). The effect of scopolamine on natural log-transformed BDNF was assessed using a mixed model, with repeated effect of time (0 minutes vs 150 minutes) and a random subject effect. All BDNF analyses included age, sex, and weight as covariates.

RESULTS

General Characteristics

Of the 23 participants enrolled into the protocol, 11 were assigned to the P/S order group and 12 were assigned to the S/P order group. Participant characteristics are presented in Table 1. There were no premature withdrawals, and all enrolled participants completed the protocol.

Primary and Secondary Outcomes

Mean MADRS scores at all assessments are shown in Figure 2. A significant effect of block was observed ($F(2,43.1) = 10.82$, $P = .0002$), explained by moderate improvements across both randomization groups from Block 0 to Block 1 (Cohen's $d = 0.85$, 95% CI: 0.22–1.47; $t(41.7) = 2.74$, $P_{\text{adj}} = .02$) and to Block 2 (Cohen's $d = 1.39$, 95% CI: 0.79–2.00; $t(43.9) = 4.62$, $P_{\text{adj}} = .0001$). The improvement from Block 1 to Block 2 exceeded the threshold for significance (Cohen's $d = 0.58$, 95% CI: -0.03–1.19; $t(101) = 2.37$, $P_{\text{adj}} = .14$).

However, no main effect or interaction with randomization was observed, indicating that scopolamine had no effect on the primary outcome (Table 2). Two of the 23 participants (one each in the S/P and P/S group) met criteria as responders during the scopolamine condition (i.e., $\geq 50\%$ improvement in MADRS from baseline to post-treatment). One of these responders also met criteria for remission (MADRS ≤ 10). One participant who responded in the scopolamine condition also met criteria for response in the placebo condition. Finally, 2 participants in the S/P group who did not respond in the scopolamine condition demonstrated remission in the placebo condition.

Four participants (2 in each of the randomization groups) did not provide data at the final assessment. To assess robustness of the results to these missing data, the 4 participants were excluded and the analysis re-run. The results did not differ (i.e., main effect of block, $P = .0017$; main effect of randomization, $P = .79$; block-by-randomization interaction, $P = .53$). Next, we analyzed the first arm of the trial, controlling for the session 2 (baseline) score. Scopolamine had no effect [$F(1,20) = 0.38$, $P = .54$], and no interaction between drug and visit [$F(2,42) = 0.01$, $P = .99$] was noted.

Similar results were observed for the secondary outcome measure, the HAM-A (Table 2). The main effect of block was significant ($F(2,42.4) = 8.33$, $P = .0009$), driven by significant improvement from Block 0 to Block 1 (Cohen's $d = 0.95$, 95% CI: 0.31–1.59; $t(39.8) = 3.01$, $P_{\text{adj}} = .005$) and to Block 2 (Cohen's $d = 1.17$, 95% CI: 0.57–1.78; $t(43.9) = 3.89$, $P_{\text{adj}} = .0003$). Change from Block 1 to Block 2 was not significant (Cohen's $d = 0.30$, 95% CI: -0.31–0.91; $t(43.8) = 0.98$, $P_{\text{adj}} = .59$).

Table 1. Subject Characteristics

	P/S (n = 11)		S/P (n = 12)		Total (N = 23)	
	M	SD	M	SD	M	SD
Age (y)	32.91	9.08	40.42	11.32	36.83	10.78
Age of onset (y)	17.3	6.96	22.5	10.22	20.14	9.08
Duration of illness (y)	14.6	10.05	17.92	13.54	16.41	11.92
MADRS	31.64	4.2	34.08	4.25	32.91	4.32
HAM-A	19	5.67	25.73	8.33	22.36	7.76
	n	%	n	%	n	%
Male	7	63	4	33	11	48
Race						
White, non-Hispanic	9	82	6	50	15	65
Black or multiracial	2	18	3	25	5	22
Unknown	0		3	25	3	13
Comorbid diagnoses						
Anxiety disorder	4	36	3	25	7	30
Obsessive compulsive disorder	0		3	25	3	13
Posttraumatic stress disorder	1	9	2	17	3	13
Personal history of alcohol/substance abuse	1	9	6	50	7	30
Medication response history						
Naïve	2	18	4	33	6	26
Resistant	7	63	8	66	15	65
Responder	2	18	0		2	9
Previous medication trials						
0–1	3	27	5	42	8	35
2–3	5	45	3	25	8	35
4–7	1	9	4	33	5	22
8+	2	18	0		2	9
Previous ECT trial	2	18	3	25	5	22

Abbreviations: ECT, electroconvulsive therapy; HAM-A, Hamilton Anxiety Rating Scale; MADRS, Montgomery-Asberg Depression Rating Scale; P/S, randomized to placebo then scopolamine; S/P, randomized to scopolamine then placebo.

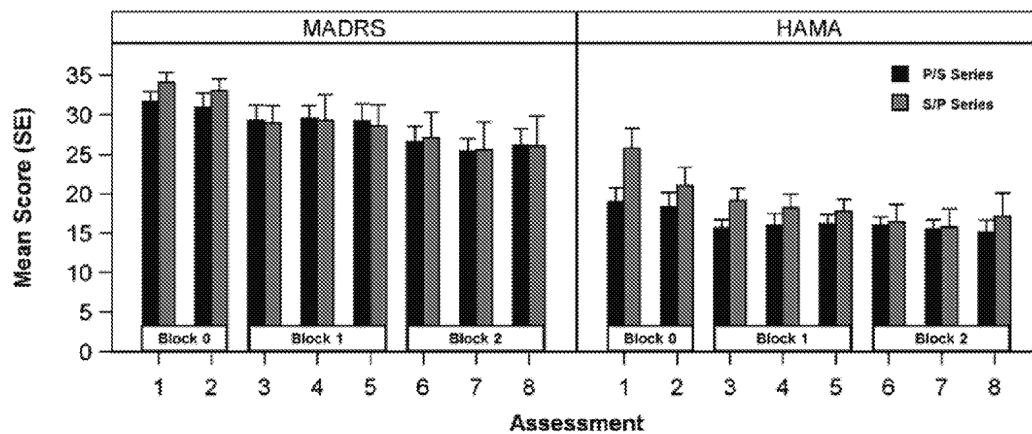


Figure 2. Montgomery-Asberg Depression Rating Scale (MADRS) and Hamilton Anxiety Rating Scale (HAM-A) scores. Assessments 4 and 7 were excluded from the analysis. Randomization group by block interaction was not significant for either scale. A main effect of block was significant for both scales. Posthoc tests indicated that for MADRS both Block 1 ($p_{adj} = .02$) and Block 2 ($p_{adj} = .0001$) differed from Block 0 but not from one another ($P_{adj} = .14$). HAM-A scores for Block 1 ($P_{adj} = .01$) and Block 2 ($P_{adj} = .001$) differed from Block 0 but not from one another ($P_{adj} = .59$). P, placebo; S, scopolamine.

Table 2. Results of Repeated-Measures ANOVA

	Num DF	Den DF	F	P
MADRS				
Block	2	43.1	10.82	.0002
Visit	1	62	0.65	.42
Group	2	62	0.09	.91
Block*visit	1	21.1	0.07	.79
Block*GROUP	2	43.1	0.65	.53
Visit*group	1	62	0.08	.78
Block*visit*group	2	62	0	1.00
HAM-A				
Block	2	42.4	8.33	.0009
Visit	1	56.9	4.72	.03
Group	1	21.3	2.29	.15
Block*visit	2	56.8	1.82	.17
Block*group	2	42.4	1.2	.31
Visit*group	1	56.9	2.59	.11
Block*visit*group	2	56.8	1.36	.26

Abbreviations: Den DF, denominator degrees of freedom; HAM-A, Hamilton Anxiety Rating Scale; Num DF, numerator degrees of freedom; MADRS, Montgomery-Asberg Depression Rating Scale.

DFs were calculated using the Satterthwaite approximation. Repeated measures nested within block were modeled with a compound symmetry variance structure and a random subject effect.

MEG Results

No significant effects of age or gender on gamma power in MDD subjects were observed, so these effects were removed from the model. There was a significant overall main effect of session (minimum $P_{FDR} = .0005$). However, this was primarily accounted for by increased gamma power in the baseline placebo-lead in session, primarily in fronto-temporal areas, and presumably due to the novelty of the scanning environment and potentially increased muscular activity. For the contrast of interest—scopolamine vs placebo—no significant effects were observed (minimum $P_{FDR} = .195$). Maps of this comparison, thresholded at $P_{uncorrected} < 0.005$, are shown in Figure 3. Gamma power was nominally increased in bilateral precuneus/angular gyrus, but nominally reduced in parahippocampal gyrus and inferior frontal gyrus.

BDNF Results

Plasma BDNF levels did not change significantly between 0 and 150 minutes under either condition (placebo, $F(1,42) = 1.78$, $P = .19$; scopolamine, $F(1,42) = 0.06$, $P = .80$) (placebo vs scopolamine, $F(1,42) = 1.26$, $P = .27$). To address the possibility of carry-over effects, data from the first block of the trial were analyzed separately (i.e., Session 2, 0 minutes vs Session 5, 0 minutes). No significant change in BDNF levels was observed following 3 infusions of placebo ($F(1,10) = 0.01$, $P = .94$) or scopolamine ($F(1,10) = 0.04$, $P = .84$) (placebo vs scopolamine, $F(1,20) = 0.04$, $P = .84$). Change in BDNF levels was not related to change in MADRS score during the first block under either condition (placebo, $t(15) = -0.35$, $P = .73$; scopolamine, $t(15) = -1.55$, $P = .14$), and this did not differ between condition (change in BDNF by condition interaction, $F(1,15) = 0.12$, $P = .73$) (see Figure 4).

Adverse Effects

Most participants reported transient minor side effects at the time of the infusions (of both scopolamine and placebo). These included expected anticholinergic side effects such as dry mouth, constipation, blurred vision, drowsiness, and nervousness. Two participants reported worsening of depression during the study; both were closely monitored and were able to complete the protocol. No unexpected or serious adverse events occurred; while a formal assessment of blinding was not conducted, clinical reports suggest that unblinding was not a major concern.

Discussion

In this randomized, placebo-controlled, crossover trial of 23 subjects with MDD, a series of 3 scopolamine infusions did not significantly improve depressive or anxiety symptoms compared with placebo. These negative results are not in line with previous studies of scopolamine for depression and suggest that the current study sample may have differed significantly from samples used in previous studies. One possible explanation for the lack of significant results in this trial may be the increased level of treatment resistance in this subject sample. While previous studies (Furey and Drevets, 2006; Drevets and Furey, 2010)

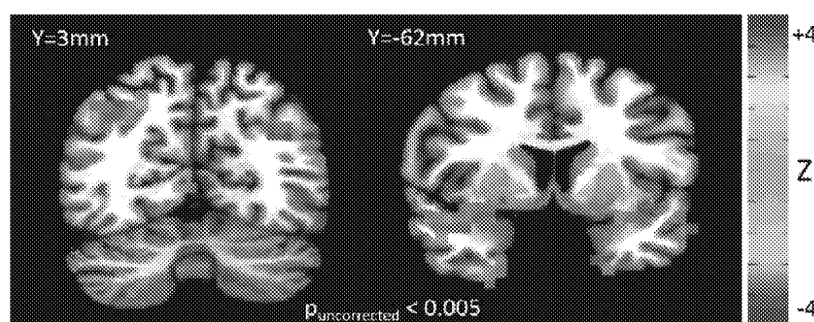


Figure 3. Z-map of the comparison of gamma power in the post-scopolamine vs post-placebo condition. Red indicates increased gamma in the scopolamine condition, and blue indicates decreased gamma in the scopolamine condition.

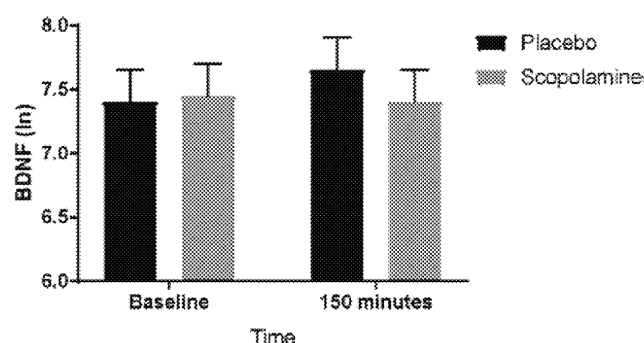


Figure 4. Results of a repeated measures model with fixed effects of time, condition, and their interaction. Least square mean estimates (with SE) are plotted. The pre-post change in natural log-transformed brain-derived neurotrophic factor (BDNF) concentrations did not differ between conditions ($F(1,42) = 1.26$, $P = .27$).

did not report data for past medication trials, the average past number of medication trials in the current study was greater than three. Furthermore, a larger proportion of patients in the previous studies were treatment naive (50% compared with 26% in the current study). Moreover, the previous studies examined wholly outpatient samples while the current study had a mix of inpatients and outpatients (7 inpatients, 16 outpatients). Another potential difference between the current and previous samples may be increased severity of depressive symptoms; specifically, average MADRS score on entering the treatment phases were between 23 and 30 in the previous studies compared with 33 in the current study.

From a translational perspective, the lack of clinical efficacy in this study did not allow us to test the hypothesis that scopolamine and ketamine have a shared mechanism of action. The results do suggest that the neurobiological effects (i.e., drug effects) of scopolamine and ketamine are at least partially distinct. It is important to acknowledge that because the response to scopolamine was small in this sample, it was not possible to assess any neurophysiological correlates of response (i.e., mechanism of action). For instance, while this cohort exhibited no drug-dependent changes in BDNF levels in response to scopolamine, it is possible that significant correlations would have been observed if clinical response had been greater. It should be noted, however, that peripheral BDNF concentrations may be difficult to interpret. For instance, in humans—though not in mice—BDNF blood levels may primarily be influenced by platelet stores, which are typically released during the coagulation process, more than brain BDNF activity (Chacon-Fernandez et al., 2016).

Regarding the neuroimaging biomarker analysis, we found no significant change in MEG gamma power following scopolamine administration in contrast to studies conducted with ketamine. For instance, both animal (Pinault, 2008; Anderson et al., 2014; Jones et al., 2014) and human (Rivolta et al., 2015; Shaw et al., 2015) studies have indicated that acute, subanesthetic doses of ketamine are associated with robust increases in gamma power regardless of clinical response. A recent study by Nugent and colleagues not only found increases in MEG gamma power in response to ketamine administration in both MDD and healthy controls, but also demonstrated a relationship between increased gamma power and antidepressant response in MDD subjects with lower baseline MEG gamma power (Nugent et al., 2018). For ketamine, it is thought that the decreased activity in GABAergic interneurons and the disinhibition of excitatory pyramidal neurons (Homayoun and Moghaddam, 2007) presumably provide the mechanism underlying these increased gamma oscillations (Carlen et al., 2012), which may function as a biomarker of antidepressant response to ketamine. The association between change in gamma power and antidepressant response could not be assessed in the current study given the lack of clinical efficacy in this cohort, and thus scopolamine's mechanism of antidepressant action could not be evaluated.

Strengths of the study include: the randomized design, the medication-free status of all the participants, the i.v. administration of the study drug (which ensures uniform administration and compliance), the 100% completion rate of the participants, the inclusion of subjects regardless of the number of past medication trials, and the inclusion of 2 distinct neurophysiological modalities obtained in relationship with treatment to scopolamine.

Taken together, these findings suggest that scopolamine may have only modest or no significant antidepressant effects in patients with more severe and treatment-resistant forms of depression. It is possible, however, that subjects who respond more robustly to scopolamine would exhibit similar neurobiological effects to those who respond to ketamine. Future studies with scopolamine in depression should factor in level of symptom severity and treatment resistance. Investigations of physiological markers associated with antidepressant response to scopolamine should be reexamined in a patient cohort that responds to this agent, as reported in previously published trials.

Funding

Funding for this work was supported by the Intramural Research Program at the NIMH, NIH (ZIA MH002927; NCT00369915), by a NARSAD Independent Investigator Award to Dr. Zarate, and by a Brain and Behavior Mood Disorders Research Award to Dr. Zarate.

Acknowledgments

The authors thank the 7SE research unit and staff for their support. Ioline Henter (NIMH) provided invaluable editorial assistance.

Statement of Interest

Dr. Zarate is listed as a co-inventor on a patent for the use of ketamine in major depression and suicidal ideation; as a co-inventor on a patent for the use of (2R,6R)-hydroxynorketamine, (S)-dehydronorketamine, and other stereoisomeric dehydro and hydroxylated metabolites of (R,S)-ketamine metabolites in the treatment of depression and neuropathic pain; and as a co-inventor on a patent application for the use of (2R,6R)-hydroxynorketamine and (2S,6S)-hydroxynorketamine in the treatment of depression, anxiety, anhedonia, suicidal ideation, and posttraumatic stress disorders. He has assigned his patent rights to the US government but will share a percentage of any royalties that may be received by the government. Dr. Furey is identified as a co-inventor on a patent in the US and Europe for the use of scopolamine as an antidepressant agent. Dr. Furey is a full-time employee at Janssen Pharmaceuticals, Neuroscience Research and Development, La Jolla, CA. All other authors have no conflict of interest to disclose, financial or otherwise.

References

- Anderson PM, Pinault D, O'Brien TJ, Jones NC (2014) Chronic administration of antipsychotics attenuates ongoing and ketamine-induced increases in cortical gamma oscillations. *Int J Neuropsychopharmacol* 17:1895–1904.
- Betin C, DeFeudis FV, Blavet N, Clostre F (1982) Further characterization of the behavioral despair test in mice: positive effects of convulsants. *Physiol Behav* 28:307–311.
- Cannon DM, Klaver JK, Ghandi SK, Solorio G, Peck SA, Erickson K, Akula N, Savitz J, Eckelman WC, Furey ML, Sahakian BJ, McMahon FJ, Drevets WC (2011) Genetic variation in cholinergic muscarinic-2 receptor gene modulates M2 receptor binding in vivo and accounts for reduced binding in bipolar disorder. *Mol Psychiatry* 16:407–418.
- Carlen M, Meletis K, Siegle JH, Cardin JA, Futai K, Vierling-Claassen D, Ruhlmann C, Jones SR, Deisseroth K, Sheng M, Moore CI, Tsai LH (2012) A critical role for NMDA receptors in parvalbumin interneurons for gamma rhythm induction and behavior. *Mol Psychiatry* 17:537–548.
- Carmichael O, Schwarz AJ, Chatham CH, Scott D, Turner JA, Upadhyay J, Coimbra A, Goodman JA, Baumgartner R, English BA, Apolzan JW, Shankapal P, Hawkins KR (2017) The role of fMRI in drug development. *Drug Discov Today* Nov 15:pii: S1359-6446(1317)30341-30340.
- Chacon-Fernandez P, Sauberli K, Colzani M, Moreau T, Ghevaert C, Barde YA (2016) Brain-derived neurotrophic factor in megakaryocytes. *J Biol Chem* 291:9872–9881.
- Chen G, Saad ZS, Britton JC, Pine DS, Cox RW (2013) Linear mixed-effects modeling approach to fMRI group analysis. *NeuroImage* 73:176–190.
- Comings DE, Wu S, Rostamkhani M, McGue M, Iacono WG, MacMurray JP (2002) Association of the muscarinic cholinergic 2 receptor (CHRM2) gene with major depression in women. *Am J Med Genet* 114:527–529.
- Cox RW (1996) AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. *Comput Biomed Res* 29:162–173.
- Dilsaver SC (1986) Pathophysiology of “cholinergic supersensitivity” in affective disorders. *Biol Psychiatry* 21:813–829.
- Drevets WC, Furey ML (2010) Replication of scopolamine’s antidepressant efficacy in major depressive disorder: a randomized, placebo-controlled clinical trial. *Biol Psychiatry* 67:432–438.
- Drevets WC, Zarate CAJ, Furey ML (2013) Antidepressant effects of the muscarinic cholinergic receptor antagonist scopolamine: a review. *Biol Psychiatry* 73:1156–1163.
- First MB, Spitzer RL, Gibbon M, Williams JBW (2001) Structured clinical interview for DSM-IV-TR axis I disorders research version, patient edition. New York, NY: Biometrics Research, New York State Psychiatric Institute.
- Furey ML, Drevets WC (2006) Antidepressant efficacy of the antimuscarinic drug scopolamine: a randomized, placebo-controlled clinical trial. *Arch Gen Psychiatry* 63:1121–1129.
- Ghosal S, Bang E, Yue W, Hare BD, Lepack AE, Girgenti MJ, Duman RS (2018) Activity-dependent brain-derived neurotrophic factor release is required for the rapid antidepressant actions of scopolamine. *Biol Psychiatry* 83:29–37.
- Gillin JC, Sutton L, Ruiz C, Darko D, Golshan S, Risch SC, Janowsky DS (1991) The effects of scopolamine on sleep and mood in depressed patients with a history of alcoholism and a normal comparison group. *Biol Psychiatry* 30:157–169.
- Gramfort A, Luessi M, Larson E, Engemann DA, Strohmeier D, Brodbeck C, Goj R, Jas M, Brooks T, Parkkonen L, Hamalainen M (2013) MEG and EEG data analysis with MNE-Python. *Front Neurosci* 7:267.
- Haile CN, Murrrough JW, Iosifescu DV, Chang LC, Al Jurdi RK, Foulkes A, Iqbal S, Mahoney J Jr, De La Garza Rn, Charney DS, Newton TF, Mathew SJ (2014) Plasma brain derived neurotrophic factor (BDNF) and response to ketamine in treatment-resistant depression. *Int J Neuropsychopharmacol* 17:331–336.
- Hare BD, Ghosal S, Duman RS (2017) Rapid acting antidepressants in chronic stress models: molecular and cellular mechanisms. *Chronic Stress* (Thousand Oaks). doi: 10.1177/2470547017697317.
- Homayoun H, Moghaddam B (2007) NMDA receptor hypofunction produces opposite effects on prefrontal cortex interneurons and pyramidal neurons. *J Neurosci* 27:11496–11500.
- Janowsky DS, el-Yousef MK, Davis JM (1974) Acetylcholine and depression. *Psychosom Med* 36:248–257.
- Janowsky DS, el-Yousef MK, Davis JM, Sekerke HJ (1972) A cholinergic-adrenergic hypothesis of mania and depression. *Lancet* 2:632–635.
- Janowsky DS, Risch SC, Huey LY, Kennedy B, Ziegler M (1985) Effects of physostigmine on pulse, blood pressure, and serum epinephrine levels. *Am J Psychiatry* 142:738–740.
- Jones NC, Anderson P, Rind G, Sullivan C, van den Buuse M, O'Brien TJ (2014) Effects of aberrant gamma frequency oscillations on prepulse inhibition. *Int J Neuropsychopharmacol* 17:1671–1681.
- Kessler RC, Petukhova M, Sampson NA, Zaslavsky AM (2012) Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. *Int J Methods Psychiatr Res* 21:169–184.
- Kishimoto T, Chawla JM, Hagi K, Zarate CA, Kane JM, Bauer M, Correll CU (2016) Single-dose infusion ketamine and non-ketamine N-methyl-D-aspartate receptor antagonists for unipolar and bipolar depression: a meta-analysis of efficacy, safety and time trajectories. *Psychol Med* 46:1459–1472.
- Li N, Lee B, Liu RJ, Banasr M, Dwyer JM, Iwata M, Li XY (2010) mTOR-dependent synapse formation underlies the rapid

- antidepressant effects of NMDA antagonists. *Science* 329:959–964.
- Machado-Vieira R, Yuan P, Brutsche N, DiazGranados N, Luckenbaugh D, Manji HK, Zarate CA Jr (2009) Brain-derived neurotrophic factor and initial antidepressant response to an N-methyl-D-aspartate antagonist. *J Clin Psychiatry* 70:1662–1666.
- Niciu MJ, Mathews DC, Nugent AC, Ionescu DF, Furey ML, Richards EM, Machado-Vieira R, Zarate CA Jr (2014) Developing biomarkers in mood disorders research through the use of rapid-acting antidepressants. *Depress Anxiety* 31:297–307.
- Nugent AC, Ballard E, Gould TD, Park LT, Moaddel R, Brutsche NE, Zarate CAJ (2018) Ketamine has distinct electrophysiological and behavioral effects in depressed and healthy subjects. *Mol Psychiatry* doi: 10.1038/s41380-018-0028-2.
- Nurnberger JI Jr, Jimerson DC, Simmons-Alling S, Tamminga C, Nadi NS, Lawrence D, Sitaram N, Gillin JC, Gershon ES (1983) Behavioral, physiological, and neuroendocrine responses to arecoline in normal twins and “well state” bipolar patients. *Psychiatry Res* 9:191–200.
- Olfson M, Blanco C, Marcus SC (2016) Treatment of adult depression in the United States. *JAMA Intern Med* 176:1482–1491.
- Overstreet DH, Russell RW, Hay DA, Crocker AD (1992) Selective breeding for increased cholinergic function: biometrical genetic analysis of muscarinic responses. *Neuropsychopharmacology* 7:197–204.
- Pinault D (2008) N-methyl d-aspartate receptor antagonists ketamine and MK-801 induce wake-related aberrant gamma oscillations in the rat neocortex. *Biol Psychiatry* 63:730–735.
- Risch SC, Kalin NH, Janowsky DS (1981) Cholinergic challenges in affective illness: behavioral and neuroendocrine correlates. *J Clin Psychopharmacol* 1:186–192.
- Rivolta D, Heidegger T, Scheller B, Sauer A, Schaum M, Birkner K, Singer W, Wibral M, Uhlhaas PJ (2015) Ketamine dysregulates the amplitude and connectivity of high-frequency oscillations in cortical-subcortical networks in humans: evidence from resting-state magnetoencephalography recordings. *Schizophr Bull* 41:1105–1114.
- Robinson SE, Vrba J (1999) Functional neuroimaging by synthetic aperture magnetometry (SAM). In: *Recent advances in biomagnetism* (Yoshimoto T, Kotani M, Kuriki S, Karibe H, Nakasato N, eds), pp302–305. Sendai: Tohoku University Press.
- Rubin RT, O’Toole SM, Rhodes ME, Sekula LK, Czambel RK (1999) Hypothalamo-pituitary-adrenal cortical responses to low-dose physostigmine and arginine vasopressin administration: sex differences between major depressives and matched control subjects. *Psychiatry Res* 89:1–20.
- Shaw AD, Saxena N, L EJ, Hall JE, Singh KD, Muthukumaraswamy SD (2015) Ketamine amplifies induced gamma frequency oscillations in the human cerebral cortex. *Eur Neuropsychopharmacol* 25:1136–1146.
- Trivedi MH, Fava M, Wisniewski SR, Thase ME, Quitkin F, Warden D, Ritz L, Nierenberg AA, Lebowitz BD, Biggs MM, Luther JF, Shores-Wilson K, Rush AJ (2006a) Medication augmentation after the failure of SSRIs for depression. *N Engl J Med* 354:1243–1252.
- Trivedi MH, Rush AJ, Wisniewski SR, Nierenberg AA, Warden D, Ritz L, Norquist G, Howland RH, Lebowitz B, McGrath PJ, Shores-Wilson K, Biggs MM, Balasubramani GK, Fava M (2006b) Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: implications for clinical practice. *Am J Psychiatry* 163:28–40.
- Voleti B, Navarria A, Liu RJ, Banasr M, Li N, Terwilliger R, Sanacora G, Eid T, Aghajanian G, Duman RS (2013) Scopolamine rapidly increases mammalian target of rapamycin complex 1 signaling, synaptogenesis, and antidepressant behavioral responses. *Biol Psychiatry* 74:742–749.
- Wang JC, et al. (2004) Evidence of common and specific genetic effects: association of the muscarinic acetylcholine receptor M2 (CHRM2) gene with alcohol dependence and major depressive syndrome. *Hum Mol Genet* 13:1903–1911.
- Wohleb ES, Gerhard D, Thomas A, Duman RS (2017) Molecular and cellular mechanisms of rapid-acting antidepressants ketamine and scopolamine. *Curr Neuropharmacol* 15:11–20.
- Zarate CA Jr, Mathews DC, Furey ML (2013) Human biomarkers of rapid antidepressant effects. *Biol Psychiatry* 73:1142–1155.
- Zarate CA Jr, Singh JB, Carlson PJ, Brutsche NE, Ameli R, Luckenbaugh DA, Charney DS, Manji HK (2006) A randomized trial of an N-methyl-D-aspartate antagonist in treatment-resistant major depression. *Arch Gen Psychiatry* 63:856–864.
- Zimmerman M, Posternak MA, Chelminski I (2004) Derivation of a definition of remission on the Montgomery-Asberg depression rating scale corresponding to the definition of remission on the Hamilton rating scale for depression. *J Psychiatr Res* 38:577–582.

From: Joe Allen [jallen@allen-assoc.com]
Sent: 1/19/2017 12:50:46 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]
Subject: KEI alleges patent failed to disclose NIH funding

Seen this:

From PatentlyO

Bayh-Dole Act: Failing to Disclose Government Funding

January 18, 2017Dennis Crouch

Interesting filing from the folks at KEI. That alleges IONIS Pharma (formerly ISIS) and Cold Springs Harbor Labs failed to disclose Federal funding supported development of the inventions underlying their patents covering nusinersen and its for the treatment of spinal muscular atrophy (SMA). See U.S. Patent Nos. 8,361,977 and 8,980,853.

The **Bayh-Dole Act** allows private entities to patent inventions developed through federal funding. However, the law requires that the federal funding be disclosed in order to allow the Government to understand and exercise its corresponding rights.

An entity that fails to disclose the funding is then subject to the penalty of title being awarded to the U.S. government – although the Government must demand title. “The Federal Government may receive title to any subject invention not disclosed to it within such time.” 35 U.S.C. § 202(c)(1).

The KEI filing is in the form of a letter to Inspector General of HHS (parent of NIH) asking for an investigation and action.

Read the Filing: [\[18jan2017-oig-investigation-request-nusinersen-patents\]](#)

If the new Trump Administration is serious about high drug prices, this may be a place to start. Nusinersen is priced at \$750,000 for the first year of treatment and \$375,000 for every year thereafter.

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

REL0000024348

From: Thomas, Gina (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=GTHOMAS]
Sent: 3/10/2015 3:09:44 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Rodriguez, Richard (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=RODRIGUR]; Ferguson, Steve (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=FERGUSOS]
CC: Sarris, Christina (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=sarrisc]; Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]
Subject: RE: FOIA Case 43496 (Cassedy) - For Input

Mark,

b5

Gina

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, March 10, 2015 11:08 AM
To: Thomas, Gina (NIH/OD) [E]; Rodriguez, Richard (NIH/OD) [E]; Ferguson, Steve (NIH/OD) [E]
Cc: Sarris, Christina (NIH/OD) [E]; Hammersla, Ann (NIH/OD) [E]
Subject: RE: FOIA Case 43496 (Cassedy) - For Input

b5

From: Thomas, Gina (NIH/OD) [E]
Sent: Tuesday, March 10, 2015 11:06 AM
To: Rodriguez, Richard (NIH/OD) [E]; Ferguson, Steve (NIH/OD) [E]
Cc: Rohrbaugh, Mark (NIH/OD) [E]; Sarris, Christina (NIH/OD) [E]; Hammersla, Ann (NIH/OD) [E]
Subject: RE: FOIA Case 43496 (Cassedy) - For Input

Richard,

b5

Gina

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, March 09, 2015 6:36 PM
To: Rodriguez, Richard (NIH/OD) [E]
Cc: Hammersla, Ann (NIH/OD) [E]; Sarris, Christina (NIH/OD) [E]; Thomas, Gina (NIH/OD) [E]; Ferguson, Steve (NIH/OD) [E]
Subject: RE: FOIA Case 43496 (Cassedy) - For Input

No. If I had any, they were deleted a long time ago. Gina had one from 2009 but that's all.

From: Rodriguez, Richard (NIH/OD) [E]
Sent: Monday, March 09, 2015 3:39 PM
To: Rohrbaugh, Mark (NIH/OD) [E]
Cc: Hammersla, Ann (NIH/OD) [E]; Sarris, Christina (NIH/OD) [E]; Thomas, Gina (NIH/OD) [E]; Ferguson, Steve (NIH/OD) [E]
Subject: RE: FOIA Case 43496 (Cassedy) - For Input

Thanks Mark. Do you have any documents that you will be able to produce?

REL0000024349

Richard

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, March 09, 2015 2:55 PM
To: Ferguson, Steve (NIH/OD) [E]; Thomas, Gina (NIH/OD) [E]; Rodriguez, Richard (NIH/OD) [E]
Cc: Hammersla, Ann (NIH/OD) [E]; Sarris, Christina (NIH/OD) [E]
Subject: RE: FOIA Case 43496 (Cassedy) - For Input

Yes, we worked on it. It was mostly an OGC, CDC and HHS issue.

From: Ferguson, Steve (NIH/OD) [E]
Sent: Monday, March 09, 2015 1:14 PM
To: Thomas, Gina (NIH/OD) [E]; Rodriguez, Richard (NIH/OD) [E]
Cc: Rohrbaugh, Mark (NIH/OD) [E]; Hammersla, Ann (NIH/OD) [E]; Sarris, Christina (NIH/OD) [E]
Subject: FW: FOIA Case 43496 (Cassedy) - For Input

Gina / Richard --

At OTT I believe that Mark worked on this issue. I don't know if he might have had Christina or Ann assist with any of it.

b5

b5

Steve

Steven M. Ferguson, CLP
Deputy Director, Licensing & Entrepreneurship
NIH Office of Technology Transfer
6011 Executive Boulevard, Suite 325
Rockville, MD 20852
Phone: (301) 435-5561
Email: sf8h@nih.gov
Web: www.ott.nih.gov

From: Thomas, Gina (NIH/OD) [E]
Sent: Monday, March 09, 2015 12:58 PM
To: Rodriguez, Richard (NIH/OD) [E]
Cc: Ferguson, Steve (NIH/OD) [E]
Subject: FW: FOIA Case 43496 (Cassedy) - For Input

Richard,

OTT just received the following FOIA request from Knowledge Ecology International (KEI).
I was unsure which group in DTDI should receive this request as they are requesting all correspondence, memoranda, talking points, powerpoints, or other communications from the National Institutes of Health relating to intellectual property rights and patent barriers involved in the development of new vaccines and drugs for possible pandemics involving:

- (1) avian influenza, and/or
- (2) requiring patents for reverse genetics(rg), and/or
- (3) taqman technologies.

REL0000024349

As regards avian influenza, this includes but is not limited to Highly Pathogenic Avian Influenza (H5N1) or Avian Influenza A (H7N9).

They are seeking:

1. Any internal NIH communications, memoranda, or documents referencing the use of government rights under the Bayh-Dole Act, including but not limited to royalty free rights to use patents or march-in rights, in relation to the development of vaccines, drugs or diagnostics.
2. NIH communications with private companies that manufacture drugs or vaccines, or universities that hold relevant patent rights, that discuss intellectual property rights issues in conjunction with pandemics and vaccines, drugs or diagnostics.
3. Any NIH communications with the White House, Office of the US Trade Representative, Department of Health and Human Services, Department of State, other federal agencies, and members of Congress and their staff concerning the Bayh-Dole Act, march-in rights, or other intellectual property issues concerning the development of vaccines, drugs or diagnostics.

Can you please advise on who should be a part of this request.

Thanks

Gina Thomas

FOIA Coordinator

Technology Transfer Policy Specialist

Office of Technology Transfer

6011 Executive Blvd; Suite 325

Rockville, MD 20852

Dir-301-435-5377

Fax-301-480-4576

gthomas@mail.nih.gov

www.ott.nih.gov

From: Bartok, Lauren (NIH/OD) [C]
Sent: Monday, March 09, 2015 12:17 PM
To: Thomas, Gina (NIH/OD) [E]
Subject: FOIA Case 43496 (Cassedy) - For Input

Gina,

Please see the attached request for OTT input. Let us know if you have any questions.

Thanks,

Lauren Bartok
Program Assistant, Contractor
Freedom of Information Office

National Institutes of Health
Building 31, Room 5B35
31 Center Drive
Bethesda, MD 20892

REL0000024349

Phone: 301-496-5633

Fax: 301-402-4541



From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 10/22/2018 3:19:59 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: What are the best answers to: [REDACTED] **b5**

See Edits below. Ann

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, October 18, 2018 3:45 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: What are the best answers to: [REDACTED] **b5**

[REDACTED] **b5**

If easier to talk, just call. [REDACTED] **b5**

[REDACTED] **b5**

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director
National Institutes of Health

From: Joe Allen [jallen@allen-assoc.com]
Sent: 7/27/2018 2:25:31 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]
Subject: 60 House Dems introduce compulsory licensing as part of Medicare reform

The beat goes on. This is from KEI's website (<https://www.keionline.org/28564>). As you can see from the highlighted section below, Jamie wants them to include march in rights and government led drug development.

60 House Democrats introduce bill on Medicare negotiations that includes compulsory licensing provisions to protect patients when price negotiations break down.

Posted on July 25, 2018 by James Love

The new House democrats medicare negotiations bill represents a turning point, with broad support for using robust compulsory licensing authority to protect access if negotiations on prices break down. The press conference announcing the bill featured several Democratic members of the House of Representatives, and patient advocates. Rob Weissman from Public Citizen gave a very strong endorsement, as did Nancy Altman from Social Security Works.

Representative Lloyd Doggett led the work on this bill, working with Representatives Welch, Cummings, Khanna and others.

KEI's view is that that medicare negotiations are quite important, and the bill takes a huge step in protecting patient interests in negotiations, but also note that 84 percent of US population and a majority of patients for many treatable diseases do not qualify for medicare.

The Democrats need to expand the compulsory licensing ambitions so that it will protect everyone from excessive prices.

The Democrats also need to understand and endorse the progressive delinking of R&D incentives from drug prices, so that access and innovation are not at odds with each other.

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

From: Soukas, Peter (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=B1F6020157AC47948C6E34166B78E433-SOUKASP]
Sent: 1/16/2019 10:34:06 PM
To: Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Puglielli, Maryann (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9f53ceacaf754875a948081bac5cc66a-pugliellim]; Williams, Richard (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e5f89fe4d27a43abb936bb20efeca3b9-rwilliams]; Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]; Mowatt, Michael (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb1ef7e2e54b4164ae34814574bda638-mmowatt]; Barnes, Mary (NIH/NIAID) [C] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=29eea0c3e3ff40f299bf2eeb40be91ce-barnesml]
Subject: RE: KEI Response Letter

Dear Dale and Mark,

Thank you both for your recent communications regarding the KEI response.

Mike Mowatt, Maryann Puglielli, Rick Williams, Suzanne Frisbie and I would like to set up a call with you to discuss the response further.

Mary Barnes of NIAID/TTIPO's administrative staff will be coordinating the call and will provide call-in information.

When is a good time for both of you?

Thank you.

Peter Soukas
National Institutes of Health
National Institute of Allergy and Infectious Diseases
Phone: 301-594-8730
Email: ps193c@nih.gov

From: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Sent: Wednesday, January 16, 2019 10:39 AM
To: Soukas, Peter (NIH/NIAID) [E] <peter.soukas@nih.gov>
Cc: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Puglielli, Maryann (NIH/NIAID) [E] <maryann.puglielli@nih.gov>; Williams, Richard (NIH/NIAID) [E] <rwilliams@niaid.nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Subject: RE: KEI Response Letter

Peter:

Mark sent you some comments on Friday with suggestions on how to improve the letter,

b5

b5

Thanks,

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47

REL0000024355

Bethesda, MD 20892

301-496-6043

301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Soukas, Peter (NIH/NIAID) [E] <peter.soukas@nih.gov>
Sent: Wednesday, January 16, 2019 10:29 AM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Cc: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Puglielli, Maryann (NIH/NIAID) [E] <maryann.puglielli@nih.gov>; Williams, Richard (NIH/NIAID) [E] <rwilliams@niaid.nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Subject: RE: KEI Response Letter

Dear Dale,

We hope everything is going well with you. We haven't received your comments/approval. Would you like to discuss further via phone? Thank you.

Peter Soukas
National Institutes of Health
National Institute of Allergy and Infectious Diseases
Phone: 301-594-8730
Email: ps193c@nih.gov

From: Soukas, Peter (NIH/NIAID) [E] <peter.soukas@nih.gov>
Sent: Thursday, January 10, 2019 5:23 PM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Puglielli, Maryann (NIH/NIAID) [E] <maryann.puglielli@nih.gov>; Williams, Richard (NIH/NIAID) [E] <rwilliams@niaid.nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Subject: KEI Response Letter

Dear Dale and Mark,

We hope everything is going well with you.

As you know, we received comments from KEI/MSF to a recent FR Notice for an exclusive license to Medigen, a vaccine company in Taiwan this past week. KEI also contacted Senator Sanders' office, who is asking for a copy of the patent application and for NIH/NIAID to extend the comment period.

Attached please find our proposed response, the FR Notice, and KEI's comment letter.

Any input you could provide would be welcome.

b5

Please contact us if you have any additional questions. Thank you.

Peter Soukas
National Institutes of Health
National Institute of Allergy and Infectious Diseases
Phone: 301-594-8730
Email: ps193c@nih.gov

REL0000024355

From: Joe Allen [jallen@allen-assoc.com]
Sent: 6/24/2017 9:20:47 PM
To: Rohrbough, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]
Subject: Why is the US Government giving a pharma giant exclusive rights to a Zika vaccine paid for by the public?

This was just posted yesterday on techdirt (<https://www.techdirt.com/blog/?tag=walter+reed+army+institute>). Note the ending where they cite Jamie Love's mischaracterization of the law as fact:

Why Is US Government Giving A Pharma Giant Exclusive Rights To A Zika Vaccine Whose Development Was Paid For By The US Public?

from the *please-tell-me-again-why-making-drugs-unaffordable-will-save-lives* dept

Here on Techdirt we've written much about the way Western pharma companies fight for their "right" to charge unaffordable prices for medicines in emerging and developing economies. In particular, they routinely take governments and local generic suppliers to court in an attempt to shore up highly-profitable monopolies on life-saving drugs. But to be fair, it's not only poorer people who are dying as a result of Big Pharma's desire to maximize profits: Western drug companies are equally happy to charge even higher prices in richer countries -- notably in the US. That's old news. But there is a pharmaceutical saga unfolding that manages to combine all the worst aspects of this kind of behavior, and to throw in a few new ones.

It concerns something really exciting and important: a vaccine that shows great promise against the devastating Zika virus, which can cause microcephaly, blindness, deafness, and calcification of the brain in children whose mothers were infected during their pregnancy. If effective, such a vaccine could be a tremendous boon not just for developing countries, but for Western ones too, since the Zika virus has already begun to spread in the US, and Europe. The vaccine was developed at the Walter Reed Army Institute for Research, and the Department of the Army funded its development. Great news, you might think: the US public paid for it, so it's only right that it should have low-cost access to it. Moreover, as an act of compassion -- and to burnish its international image -- the US could allow other countries to produce it cheaply too. But an article in The Nation reports that the US Army has other ideas:

the Army is planning to grant exclusive rights to this potentially groundbreaking medicine -- along with as much as \$173 million in funding from the Department of Health and Human Services -- to the French pharmaceutical corporation Sanofi Pasteur. Sanofi manufactures a number of vaccines, but it's also faced repeated allegations of overcharges and fraud. Should the vaccine prove effective, Sanofi would be free to charge whatever it wants for it in the United States. Ultimately, the vaccine could end up being unaffordable for those most vulnerable to Zika, and for cash-strapped states.

The Knowledge Ecology Institute (KEI), led by Jamie Love, made a reasonable suggestion to ensure that those most at need would have access to the drug at a reasonable price. KEI asked that, if Sanofi does get an exclusive deal, it should be obliged to make the vaccine available at an affordable price. The Army said it lacked the ability to enforce price controls, but it would ask those nice people at Sanofi to commit to affordable pricing on a voluntary basis. According to The Nation, those nice people at Sanofi refused. Speaking of nice people at Sanofi, the article notes the following:

Sanofi's record also includes a number of controversies related to its pricing practices, from a \$190 million fine to settle charges that it defrauded Medicare and other government programs, to a \$109 million fine to settle charges that it illegally provided product kickbacks to doctors. In 2014, a whistle-blower alleged the company engaged in another kickback scheme and the destruction of legal evidence. KEI maintains a comprehensive list of Sanofi's fraud fines, including the latest: a \$19.9 million settlement, reached this April, for overcharging the Department of Veterans' Affairs.

When there is an entire Web page dedicated to listing Sanofi's problems going back to 2009, you really have to wonder why the US Army is so keen to give the company a monopoly on this promising new treatment. The usual argument for the sky-high prices of drugs is that firms must be rewarded for taking on the financial risk of drug development, otherwise they won't proceed, and the world would be the poorer. Except, of course, in this case that risk was entirely borne by the US public, which paid for the early stage development of the vaccine with their taxes. So Sanofi risked nothing, but now looks likely to reap the benefits by being allowed to price the vaccine out of the reach of the people who most need it. You might think there ought to be a law against this kind of behavior. It turns out that there is:

KEI's Jamie Love pointed out that under the Bayh-Dole Act of 1980, it is already illegal to grant exclusive rights to a federally owned invention unless the license holder agrees to make it available at reasonable pricing. But that provision has rarely, if ever, been enforced.

Now would be a really great time to start enforcing that law.

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

From: Mowatt, Michael (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CB1EF7E2E54B4164AE34814574BDA638-MMOWATT]
Sent: 10/17/2017 4:49:54 PM
To: Routh, Jennifer (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e3b5bba3619344e38037ca94a71473a8-routhj]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Stover, Kathy (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c82722674ba14c2f969bd50dfa6a7af4-stoverk]; Mowatt, Michael (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb1ef7e2e54b4164ae34814574bda638-mmowatt]; Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]
Subject: RE: For awareness
Attachments: Questions from Ed Silverman at STAT (002) ks MMowatt 171017.docx

See my comments tracked.

Mark will chime in with changes/additions if he has any.

In the future please do not hesitate to specify a deadline when you need our response. It helps us prioritize.

From: Routh, Jennifer (NIH/NIAID) [E]
Sent: Tuesday, October 17, 2017 10:39 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>
Cc: Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>
Subject: RE: For awareness

Mark, Mike and Suzanne –

Thanks for your input. We've drafted a response to the reporter (attached) with a few questions in the margin. Please let us know what you think.

Thanks,
Jen

Jennifer Routh [E]
Scientific Communications Editor
Office of Communications and Government Relations
National Institute of Allergy and Infectious Diseases (NIAID)
NIH/HHS
31 Center Drive Room 7A17B
Bethesda, MD 20892
Direct: (301) 496-8327
jennifer.routh@nih.gov

Disclaimer: The information in this e-mail and any of its attachments is confidential and may contain sensitive information. It should not be used by anyone who is not the original intended recipient. If you have received this e-mail in error please inform the sender and delete it from your mailbox or any other storage devices. The National Institute of Allergy and Infectious Diseases shall not accept liability for any statements made that are sender's own and not expressly made on behalf of the NIAID by one of its representatives.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, October 17, 2017 10:11 AM
To: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>; Billet, Courtney (NIH/NIAID) [E] <billetc@niaid.nih.gov>; Fauci, Anthony (NIH/NIAID) [E] <afauci@niaid.nih.gov>

REL0000024357

Cc: Mascola, John (NIH/VRC) [E] <jmascola@mail.nih.gov>; Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>; Routh, Jennifer (NIH/NIAID) [E] <jennifer.routh@nih.gov>; Conrad, Patricia (NIH/NIAID) [E] <conradpa@niaid.nih.gov>; Folkers, Greg (NIH/NIAID) [E] <gfolkers@niaid.nih.gov>
Subject: RE: For awareness

I agree.

b5

b5

From: Mowatt, Michael (NIH/NIAID) [E]

Sent: Tuesday, October 17, 2017 10:05 AM

To: Billet, Courtney (NIH/NIAID) [E] <billetc@niaid.nih.gov>; Fauci, Anthony (NIH/NIAID) [E] <afauci@niaid.nih.gov>

Cc: Mascola, John (NIH/VRC) [E] <jmascola@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>;

Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>; Routh, Jennifer (NIH/NIAID) [E] <jennifer.routh@nih.gov>;

Conrad, Patricia (NIH/NIAID) [E] <conradpa@niaid.nih.gov>; Folkers, Greg (NIH/NIAID) [E] <gfolkers@niaid.nih.gov>;

Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>

Subject: RE: For awareness

Regarding Q2:

b5

Having said this, the starting point for the license negotiation will be a publicly available "NIH model" license agreement (see <https://www.ott.nih.gov/resources#MLA>, "Exclusive patent license agreement"), the majority of the terms of which usually remain unmodified. The appendices include the most sensitive information.

Mark may have additional comments.

Mike

From: Billet, Courtney (NIH/NIAID) [E]

Sent: Tuesday, October 17, 2017 9:05 AM

To: Fauci, Anthony (NIH/NIAID) [E] <afauci@niaid.nih.gov>

Cc: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>; Mascola, John (NIH/VRC) [E] <jmascola@mail.nih.gov>;

Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>; Routh,

Jennifer (NIH/NIAID) [E] <jennifer.routh@nih.gov>; Conrad, Patricia (NIH/NIAID) [E] <conradpa@niaid.nih.gov>; Folkers,

Greg (NIH/NIAID) [E] <gfolkers@niaid.nih.gov>

Subject: For awareness

We have been contacted by STAT's Ed Silverman, author of the piece below from May re Sanofi deal.

We have sent him the Fed Reg notice, and are now working on answers to some follow-up questions, which are (1) why an ***exclusive*** license and (2) assuming we proceed with licensure, will the terms be disclosed. We have the answer to the first question and are seeking the answer to the second. He is not requesting an interview.

<https://www.statnews.com/2017/05/29/zika-vaccine-price/>

REL0000024357

US taxpayers are funding a Zika vaccine. Let's make sure US patients can afford it

By ED SILVERMAN

MAY 29, 2017

Dear Acting Secretary Speer,

As you know, the United States must prepare for future outbreaks of the Zika virus, but a high-stakes debate has erupted over a deal the federal government may strike with a private company to develop a vaccine. As acting secretary of the US Army, you have an opportunity — and responsibility — to find a workable solution.

The issue is whether the company — in this case, Sanofi Pasteur — should be required to make the vaccine, which is based on technology discovered with US taxpayer funds, affordable for Americans in return for an exclusive license to develop it into a commercial product.

I understand there are risks, but you should find a way to ensure that Americans do not overpay.

Here's the backstory: Last year, the government gave Sanofi, which is one of the world's largest vaccine makers, a \$43 million grant. Another \$130 million may follow as research continues. The Army also disclosed plans to award Sanofi an exclusive license to a pair of patents that are crucial to the vaccine.

But this move upset some lawmakers and patient advocates, who fear the deal will give the company a monopoly to exploit — and might lead Sanofi to jack up prices for American consumers, assuming the virus spreads and vaccines actually become a big market.

The backdrop to such concerns is the larger controversy over the rising cost of prescription medicines, a problem that has upset many Americans, prompted a flurry of legislation, and put the pharmaceutical industry on the defensive.

Sanofi, which is already under fire over its insulin pricing, is well-aware of the problem. Earlier this month, the company sought to deflect criticism — and mounting negative publicity — by vowing to limit price hikes for its medicines to a level at or below the rate of medical inflation in the US.

But an advocacy group, Knowledge Ecology International, argued Sanofi cannot be trusted and pointed to pricing for its Aubagio multiple sclerosis drug. Americans using a coupon can pay about \$6,100 for a month's supply — which is seven times more than patients pay in France and at least four times the price in the UK, Ireland, and Australia. A Sanofi spokeswoman says prices vary due to circumstances in each country.

This is why Senator Bernie Sanders and others maintain the Army should push Sanofi for fair pricing on the Zika vaccine. They want a guarantee that Americans would pay a price comparable to what other countries are charged. But as you know, Secretary Speer, Sanofi rejected such a request from your staff last month.

Drug makers generally avoid discussing pricing decisions in advance and Sanofi is no exception. In this case, the company has noted the vaccine doesn't even exist yet.

A Sanofi executive offered further insight in a letter to a House subcommittee last week. "Given the high risk nature of vaccine development and unpredictability for diseases like Zika, if the US government changes its historic approach to licensing terms, it could undermine the intent of these types of collaborations," wrote Adam Gluck, who heads US government relations for the drug maker.

In other words, if a company is forced to agree to certain pricing constraints in advance, it may not bother working with the government to develop such vaccines in the first place.

Indeed, this risk that companies might respond in this way has long worried government officials. In 1995, in fact, the National Institutes of Health removed what was called a "reasonable pricing" clause from research agreements with companies. At the time, former NIH Director Harold Varmus described such clauses as a "restraint" on new product development.

"What companies don't like is additional uncertainty for commercial considerations piled on top of the inherent risk of doing drug development," said Genia Long, a senior advisor at Analysis Group, an economic and strategic consulting firm. "If the federal government is going to insert pricing considerations, it might affect their willingness to enter into such agreements."

I understand that such notions may give your negotiating team second thoughts. Playing hardball in a situation where public health is at stake is not easy.

But while you may be worried that Sanofi could walk away if pressed too hard on pricing, consider that the company also has something to lose — it would be turning its back on a potentially money-making vaccine that can be sold in numerous markets around the world.

In an era of rising drug costs — an issue that your boss has insisted must be solved — you have an opportunity to ensure that tax dollars spent subsidizing research provide a return on investment that benefits all Americans.

Questions from Ed Silverman at STAT:

Why is an exclusive license going to be granted?

And will the terms be disclosed?

NIAID Response (attributed generally to NIAID):

b5

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 10/23/2018 7:01:37 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Merritt, William (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=33aed7eef02943408617245830eb07a8-merrittw]
Subject: FW: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

Bill and Mark: The following is DFCI response to my email regarding the questions/issues we had.

Ann

From: Sclar, Gary M. <Gary_Sclar@DFCI.HARVARD.EDU>
Sent: Monday, October 22, 2018 2:49 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Libka, Hilary <Hilary_Libka@DFCI.HARVARD.EDU>; Rice Ackman, Rachel E. <Rachel_RiceAckman@DFCI.HARVARD.EDU>; Summa, Liza <Liza_Summa@DFCI.HARVARD.EDU>; Lowe, David S. <David_Lowe@DFCI.HARVARD.EDU>
Subject: RE: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

Dear Ms. Hammersla:

DFCI appreciates this opportunity and is providing a response by the date requested, but we reiterate that a phone conversation would be useful and appreciated in order to better understand the perspective of the NIH Program Officer. Please contact us at your earliest convenience to schedule a time to discuss.

b4

Regards,

REL0000024359

Gary

Gary M. Sclar, J.D.
Vice President, Dana-Farber Innovations
Dana-Farber Cancer Institute
Belfer Office for Dana-Farber Innovation
450 Brookline Ave., Boston, MA 02215
Phone: 617-632-5807 • Fax: 617-632-4012
Email: gary_sclar@dfci.harvard.edu

From: Sclar, Gary M.
Sent: Monday, October 15, 2018 6:02 PM
To: 'Hammersla, Ann (NIH/OD) [E]' <hammerslaa@mail.nih.gov>
Cc: Libka, Hilary <Hilary_Libka@DFCI.HARVARD.EDU>; Rice Ackman, Rachel E. <Rachel_RiceAckman@DFCI.HARVARD.EDU>; Summa, Liza <Liza_Summa@DFCI.HARVARD.EDU>; Lowe, David S. <David_Lowe@DFCI.HARVARD.EDU>
Subject: RE: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

Dear Dr. Hammersla,

I just wanted to follow-up on my email below as beginning the end of next week, due to travel, we may have some scheduling issue to navigate on our side.

Regards,

Gary

From: Sclar, Gary M.
Sent: Tuesday, October 09, 2018 1:34 PM
To: 'Hammersla, Ann (NIH/OD) [E]' <hammerslaa@mail.nih.gov>
Cc: Libka, Hilary <Hilary_Libka@DFCI.HARVARD.EDU>; Rice Ackman, Rachel E. <Rachel_RiceAckman@DFCI.HARVARD.EDU>; Summa, Liza <Liza_Summa@DFCI.HARVARD.EDU>; Lowe, David S. <David_Lowe@DFCI.HARVARD.EDU>
Subject: RE: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

Dear Dr. Hammersla,

It may be useful to coordinate a phone a call to elaborate on our response and answer any questions you may have. If you agree, we would be happy to schedule such a call at your earliest convenience.

Regards,

Gary

Gary M. Sclar, J.D.
Vice President, Dana-Farber Innovations
Dana-Farber Cancer Institute
Belfer Office for Dana-Farber Innovation
450 Brookline Ave., Boston, MA 02215

REL0000024359

Phone: 617-632-5807 • Fax: 617-632-4012
Email: gary_sclar@dfci.harvard.edu

From: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Sent: Monday, October 01, 2018 2:04 PM
To: Sclar, Gary M. <Gary_Sclar@DFCI.HARVARD.EDU>
Subject: FW: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

External Email - Use Caution

Dear Dr. Scala:

Thank you for your April 25, 2018 detailed response to my email dated April 12, 2018 regarding the DFCI's and Dr. James Griffin's inventions and the commercialization of Rydapt®

NIH has continued its research into the questions that have been raised and reviewed the statement of research for NIH Grant PO 066996. NIH's Program Officer was unable to confirm the aims to this referenced NIH grant as you summarized in your April 25, 2018 response. NIH's Program Officer found the following were the aims for CA066996-06.

b4

With this updated information on the aims of CA066996 could you please review again and assess the use of NIH's funding support for the development of Rydapt®. Also please assess again if the results of this NIH funding led to the testing of the formulation that led to Rydapt®.

A second publication published by the American Society of Hematology entitled: "*Patients with acute myeloid leukemia and an activating mutation of FLT3 respond to a small-molecule FLT3 tyrosine kinase inhibitor, PKC412*" cites CA 066996 as "supporting in part" the research supported. Attached is a copy of this paper.

Please provide me with Dana Farber's assessment of these updates by October 22, 2018. If you have any questions, please let me know

Ann Hammersla

-

Ann M. Hammersla, J.D.
Director
Division of Extramural Inventions and Technology Resources
Office of Policy for Extramural Research Administration
Rockledge 1, Suite 310
6705 Rockledge Drive
Bethesda, Maryland 20892-7974
PHONE: 301-435-0745

From: Sclar, Gary M. <Gary_Sclar@DFCI.HARVARD.EDU>
Sent: Wednesday, April 25, 2018 3:00 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Rice Ackman, Rachel E. <Rachel_RiceAckman@DFCI.HARVARD.EDU>; Libka, Hilary <Hilary_Libka@DFCI.HARVARD.EDU>
Subject: RE: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

Dear Ms. Hammersla,

Attached please find the details of our evaluation of the above-referenced patents and NIH Grants P01 CA066996 and RC1 CA147386, as you requested.

As a result of our evaluation, DFCI appropriately did not report that federal funding was used in the conception or reduction to practice of the subject matter of the patents. We are happy to set up a call to discuss further, if this would be useful to you.

Regards,

Gary

Gary M. Sclar, J.D.
Vice President, Dana-Farber Innovations
Dana-Farber Cancer Institute
Belfer Office for Dana-Farber Innovation
450 Brookline Ave., Boston, MA 02215
Phone: 617-632-5807 • Fax: 617-632-4012
Email: gary_sclar@dfci.harvard.edu

REL0000024359

From: Sclar, Gary M.
Sent: Thursday, April 12, 2018 1:59 PM
To: 'Hammersla, Ann (NIH/OD) [E]' <hammerslaa@mail.nih.gov>
Cc: Rice Ackman, Rachel E. <Rachel_RiceAckman@DFCI.HARVARD.EDU>; Libka, Hilary <Hilary_Libka@DFCI.HARVARD.EDU>
Subject: RE: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

Dear Ms. Hammersla,

Thank you for your email. DFCI is aware of KEI's concerns related to grants P01 CA066996 and RC1 CA147386. We have been reviewing this matter internally and plan to provide you with the results of that evaluation by April 25, 2018, as requested.

Regards,

Gary

Gary M. Sclar, J.D.
Vice President, Dana-Farber Innovations
Dana-Farber Cancer Institute
Belfer Office for Dana-Farber Innovation
450 Brookline Ave., Boston, MA 02215
Phone: 617-632-5807 • Fax: 617-632-4012
Email: gary_sclar@dfci.harvard.edu

From: Hammersla, Ann (NIH/OD) [E] [<mailto:hammerslaa@mail.nih.gov>]
Sent: Thursday, April 12, 2018 8:33 AM
To: Sclar, Gary M. <Gary_Sclar@DFCI.HARVARD.EDU>
Subject: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

Dear Mr. Sclar:

On March 21, 2018 Knowledge Ecology International (KEI) brought to the National Institutes (NIH) attention its findings that NIH funding to the Dana-Farber Cancer Institute (Dana-Farber) for Dr. James Griffin was used in the development of the inventions that led to two United States patents referenced above. These patents identify Dr. Griffin as an inventor and were issued jointly to Dana-Farber and Novartis AG. The Food and Drug Administration's Orange Book identifies these patents as being used in the manufacture of Rydapt® (INN midostaurin).

Two NIH grants, P01 CA066996 and RC1 CA147386, have been identified as sources of research funding that may have led to the conception or the reduction to practice of the subject inventions that led to these two patents. Dana Farber disclosed to NIH 18 subject inventions in iEdison with Dr. Griffin as an inventor but has not reported the issuance of these two identified patents.

KEI, in its attached March 21, 2018 letter requests that NIH take title to these two identified patents in accordance with 37 C.F.R. § 401.14(a)(d), require U.S. Manufacturing as required by 37 C.F.R. § 401.14(a)(i), and/or or based on NIH's findings of Dana-Farber's lack of compliance in disclosing or acknowledging NIH support of the two patents in question use NIH's rights as set forth at 37 C.F.R. § 401.14(a)(j).

As part of the NIH's Bayh-Dole Act oversight responsibilities, NIH requests that within ten business days of the date of this email, Dana-Farber provide detailed information concerning NIH's research funding to Dana-Farber for research by Dr. Griffin, including the two NIH grants cited above, and its evaluation of whether federal funding was used in the conception or reduction to practice of the inventions that led to the granting of these two patents.

If you have any questions, you can contact me at the number and email address below.

Ann Hammersla

--

Ann M. Hammersla, J.D.

Director

Division of Extramural Inventions and Technology Resources

Office of Policy for Extramural Research Administration

Rockledge 1, Suite 310

6705 Rockledge Drive

Bethesda, Maryland 20892-7974

PHONE: 301-435-0745

The information in this e-mail is intended only for the person to whom it is addressed. If you believe this e-mail was sent to you in error and the e-mail contains patient information, please contact the Partners Compliance HelpLine at <http://www.partners.org/complianceline> . If the e-mail was sent to you in error but does not contain patient information, please contact the sender and properly dispose of the e-mail.

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 5/8/2018 5:22:38 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: Legal/regulatory restrictions on transfers of NIH-funded IP

From: Andrew Goldman <andrew.goldman@keionline.org>
Sent: Tuesday, May 08, 2018 11:28 AM
To: Rogers, Karen (NIH/OD) [E] <RogersK@od.nih.gov>
Cc: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; robert.silverman@oxfam.org; Jamie Love <james.love@keionline.org>
Subject: Re: Legal/regulatory restrictions on transfers of NIH-funded IP

Dear Ms. Rogers: Thank you for your quick reply. We would be interested in discussing both scenarios.

Best,
Andy

--
Andrew S. Goldman
Counsel, Policy and Legal Affairs
Knowledge Ecology International
andrew.goldman@keionline.org // www.twitter.com/ASG_KEI
tel.: +1.202.332.2670
www.keionline.org

On Mon, May 7, 2018 at 4:49 PM, Rogers, Karen (NIH/OD) [E] <rogersk@od.nih.gov> wrote:

Hi Mr. Goldman – My office would not be the appropriate one to discuss this with you. I would like to direct you to the correct staff at the NIH. Can you let me know if the NIH-funded intellectual property was supported through grants or if the technology was developed at the NIH and licensed? Regards, Karen

Karen L. Rogers

Acting Director

Office of Technology Transfer

National Institutes of Health

6011 Executive Boulevard, Suite 325

Rockville, MD 20852

E-Mail: RogersK@nih.gov

REL0000024361

Phone: 301-435-4359

Fax: 301-402-8678

From: Andrew Goldman [mailto:andrew.goldman@keionline.org]

Sent: Monday, May 07, 2018 4:11 PM

To: Rogers, Karen (NIH/OD) [E] <rogersk@od.nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>

Cc: robert.silverman@oxfam.org; Jamie Love <james.love@keionline.org>

Subject: Legal/regulatory restrictions on transfers of NIH-funded IP

Dear Karen, Ann:

I have cc'd Robert Silverman of Oxfam, and James Love of KEI, as we had hoped to have a conversation with you regarding the NIH's authority to restrict offshore transfers of NIH-funded intellectual property from a company to a subsidiary or affiliate.

Would you have time for a phone call on this? If there is a different office in NIH that you think would be more appropriate for this conversation, please let us know.

Kind regards,

Andrew S. Goldman

Counsel, Policy and Legal Affairs

Knowledge Ecology International

andrew.goldman@keionline.org // www.twitter.com/ASG_KEI

tel.: [+1.202.332.2670](tel:+12023322670)

www.keionline.org

REL0000024361

From: Yang, Jasmine (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DCACD5B675E74725A0D6A6FC9A130431-YANGJJ2_6B5]
Sent: 1/11/2019 9:26:32 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]
CC: Rodriguez, Richard (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8092cb5394e04733ac0d4d84d25f65e5-rodrigr]; Thomas, Jeffrey (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f7b9fca6f5634a45ba8802d6f6c8a410-jeffreyt]
Subject: RE: KEI Response to Jasmine's FRN
Attachments: RE: Prospective Grant of an Exclusive Patent License: "Multifunctional RNA Nanoparticles and Methods of Uses" and "RNA/DNA Hybrid Nanoparticles Modified With Single Stranded RNA Toeholds and Uses Thereof", to Sixfold Biosciences Inc.

Here you go.
I've also attached the letter and email in Tech Tracs.
Have a nice weekend.
Jasmine

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, January 11, 2019 3:08 PM
To: Yang, Jasmine (NIH/NCI) [E] <jasmine.yang@nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Thomas, Jeffrey (NIH/NCI) [E] <jeffreyt@mail.nih.gov>
Subject: RE: KEI Response to Jasmine's FRN

Please send me a copy of the final. Thanks

From: Yang, Jasmine (NIH/NCI) [E] <jasmine.yang@nih.gov>
Sent: Friday, January 11, 2019 3:02 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Thomas, Jeffrey (NIH/NCI) [E] <jeffreyt@mail.nih.gov>
Subject: RE: KEI Response to Jasmine's FRN

I'm comfortable with this change. I'll make the change and send it to KEI.
Thanks,
Jasmine

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, January 11, 2019 2:59 PM
To: Yang, Jasmine (NIH/NCI) [E] <jasmine.yang@nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Thomas, Jeffrey (NIH/NCI) [E] <jeffreyt@mail.nih.gov>
Subject: RE: KEI Response to Jasmine's FRN

b5

b5

From: Yang, Jasmine (NIH/NCI) [E] <jasmine.yang@nih.gov>
Sent: Friday, January 11, 2019 2:40 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Thomas, Jeffrey (NIH/NCI) [E] <jeffreyt@mail.nih.gov>
Subject: FW: KEI Response to Jasmine's FRN

Hi Dale and Mark,

Thanks for cleaning up the KEI letter.

b5

b5

Let me know if you disagree.

Thanks,
Jasmine

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, January 10, 2019 1:06 PM
To: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Cc: Yang, Jasmine (NIH/NCI) [E] <jasmine.yang@nih.gov>; Thomas, Jeffrey (NIH/NCI) [E] <jeffreyt@mail.nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: RE: KEI Response to Jasmine's FRN

Thanks Richard. Dale and I have reviewed this and have suggested changes

b5

b5

From: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Sent: Thursday, January 10, 2019 9:00 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Yang, Jasmine (NIH/NCI) [E] <jasmine.yang@nih.gov>; Thomas, Jeffrey (NIH/NCI) [E] <jeffreyt@mail.nih.gov>
Subject: KEI Response to Jasmine's FRN

Hi Mark,

b5

b5

b5

Please let us know if you have additional thoughts.

Thanks,

Richard

RICHARD U. RODRIGUEZ
Associate Director
Patent Agent

Technology Transfer Center
National Cancer Institute
National Institutes of Health
9609 Medical Center Drive, Rm 1E530
Bethesda, MD 20892-9702 (for business mail)
Rockville, MD 20850-9702 (for courier service/visitors)
Phone (Main Office): 240-276-5530
Direct phone: 240-276-6661
Fax 240-276-5504
richard.rodriguez@nih.gov
<https://techtransfer.cancer.gov>

"Start by doing what's necessary; then do what's possible; and suddenly you are doing the impossible" - Francis of Assisi

Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, copying or use of this email or the information enclosed therein is strictly prohibited, and you should notify the sender for return of any attached documents.

REL0000024364

From: Yang, Jasmine (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DCACD5B675E74725A0D6A6FC9A130431-YANGJJ2_6B5]
Sent: 1/11/2019 8:10:58 PM
To: James Love [james.love@keionline.org]
CC: Claire Cassedy [claire.cassedy@keionline.org]; Alex Lawson [alawson@socialsecurityworks.org]; Brook Baker [b.baker@northeastern.edu]; Manon Ress [MANON.RESS@cancerunion.org]
Subject: RE: Prospective Grant of an Exclusive Patent License: "Multifunctional RNA Nanoparticles and Methods of Uses" and "RNA/DNA Hybrid Nanoparticles Modified With Single Stranded RNA Toeholds and Uses Thereof", to Sixfold Biosciences Inc.
Attachments: 2019-01-11_LetterToKEI.pdf

Dear Mr. Love,

Thank you for your emails. Please see attached letter addressing your comments.

Sincerely,
Jasmine

From: James Love <james.love@keionline.org>
Sent: Monday, January 7, 2019 4:53 PM
To: Yang, Jasmine (NIH/NCI) [E] <jasmine.yang@nih.gov>
Cc: Claire Cassedy <claire.cassedy@keionline.org>; Alex Lawson <alawson@socialsecurityworks.org>; Brook Baker <b.baker@northeastern.edu>; Manon Ress <MANON.RESS@cancerunion.org>
Subject: Prospective Grant of an Exclusive Patent License: "Multifunctional RNA Nanoparticles and Methods of Uses" and "RNA/DNA Hybrid Nanoparticles Modified With Single Stranded RNA Toeholds and Uses Thereof", to Sixfold Biosciences Inc.

January 7, 2018

Jasmine Yang, PhD
Senior Licensing and Patenting Manager
NCI Technology Transfer Center
9609 Medical Center Drive, RM 1E530 MSC 9702
Bethesda, MD 20892-9702
Via Email: jasmine.yang@nih.gov

Re: 83 FR 65694, Prospective Grant of an Exclusive Patent License: "Multifunctional RNA Nanoparticles and Methods of Uses" and "RNA/DNA Hybrid Nanoparticles Modified With Single Stranded RNA Toeholds and Uses Thereof", to Sixfold Biosciences Inc.

Dear Dr. Jasmine Yang,

We are writing to express opposition to an exclusive license on the patent portfolio described in 83 FR 65694, regarding "Multifunctional RNA Nanoparticles and Methods of Uses" and "RNA/DNA Hybrid Nanoparticles Modified With Single Stranded RNA Toeholds and Uses Thereof," to Sixfold Biosciences Inc.

We note that Sixfold Biosciences, although recently incorporated in California, is a United Kingdom-based start-up company, and does not have a record of successful development of any technology. The web page at <https://www.sixfold.bio/> has only a few pages. The company Twitter account (https://twitter.com/sixfold_bio) was created in April 2018, and as of this morning, had 47 tweets,

mostly linked to promotional stories about the founders. LinkedIn lists four employees, one from Italy and three from the UK.

We consulted with, and concur with, the findings of an expert advisor, who reviewed the Federal Register Notice and stated that a broad exclusive license is inappropriate for a platform technology.

“For a platform technology, unless the company is founded around the platform (which is not the case here), I think a license that is exclusive in a field — ideally defined by a specified indication (not all cancer, but specific to tumor type) — is more appropriate. This preserves the commercial benefit for a therapeutic product while still encouraging licenses for other therapies for other diseases.”

In the event that the NIH makes the enormous mistake of giving a small UK start-up company a broad worldwide monopoly on a platform technology developed at the NIH, we ask that the following safeguards be placed on the license.

1. Any products using the patented invention should be available in the United States at a price that does not exceed the median price in the seven largest economies by GDP that have at least 50 percent of the GNI per capita as the United States, using the World Bank Atlas method. This is a modest safeguard for a license to a UK company. We note that UK (and other foreign) companies have a long history of charging higher prices in the United States than in the UK or other high income countries.
2. The exclusive license does not extend to countries with a per capita income less than 30 percent of the United States, in order to ensure that the patents do not lead to restricted and unequal access in developing countries.
3. Reduce term of exclusivity when revenues are large. We propose that the exclusivity of the license be reduced when the global cumulative sales from products or services using the inventions exceed certain benchmarks. This request is consistent with the statutory requirements of 35 USC § 209, which requires that “the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application.” One possible implementation of revenue benchmarks is as follows: exclusivity for any specific product or service will be reduced by one year for every \$500 million in revenue equivalents, earned after the first \$1 billion, where revenue equivalent is defined as global cumulative sales for the specific product or service, plus any market entry rewards, the cash value of priority review vouchers, as well as government grants or tax credits, for the product or service using the invention. However, the NIH could choose different benchmarks, so long as the limits on exclusivity address the requirements of 35 USC § 209, that the incentive is “not greater than reasonably necessary.”
4. The licensee should be required to file an annual report to the NIH, available to the public, on the research and development (R&D) costs associated with the development of any product or service that uses the inventions, including reporting separately and individually the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward the company be required to report on actual R&D outlays to develop the subject inventions. Reporting on actual R&D outlays is important for determining if the NIH is meeting the requirements of 35 USC § 209, that “the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical

application.” Specifically, having data on actual R&D outlays on each clinical trial used to obtain FDA approval provides evidence that is highly relevant to estimating the risk adjusted costs of bringing NIH licensed inventions to practical application.

Sincerely,

James Love
james.love@keionline.org

on behalf of:

HealthGap
Knowledge Ecology International (KEI)
Social Security Works (SSI)
Union for Affordable Cancer Treatment (UACT)

Professor Brook Baker, School of Law, Northeastern University
James Love

--

James Love. Knowledge Ecology International
<http://www.keionline.org>
twitter.com/jamie_love



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health/ NCI
8490 Progress Drive
Riverside 5 building, Suite 400
Frederick, MD 21701
Phone (301) 624-8775
FAX (301) 631-3033

Via email only

January 11, 2019

Mr. James Love
Knowledge Ecology International
1621 Connecticut Avenue NW, Suite 500
Washington, DC 20009

IN RE: Prospective Grant of an Exclusive Patent License: "Multifunctional RNA Nanoparticles and Methods of Uses" and "RNA/DNA Hybrid Nanoparticles Modified with Single Stranded RNA Toeholds and Uses Thereof", Noticed at Federal Register / Vol. 83, No. 245 / Friday, December 21, 2018

Dear Mr. Love:

Thank you for your emails dated December 25, 2018 (two emails) and January 07, 2019 (two emails) with your comments regarding the above-referenced Federal Register Notice of the proposed [Startup Exclusive Evaluation License](#) the National Cancer Institute intends to grant to Sixfold Biosciences Inc., a U.S.-based startup company.

With respect to your comment regarding the grant of an exclusive license for use of the technologies in gene-editing or drug delivery, the NIH has determined that the criteria set forth in 37 CFR 404.7(a)(1)(ii-iii) have been satisfied in view of the applicant's intentions, plans and abilities to bring the invention to the point of practical application. We believe that the company is qualified both technically and financially to be granted an exclusive license to the Government's intellectual property in the field of use as specified. Our long experience in licensing these technologies, supplemented as it always is by responses to our license notices and our understanding of the commercial market in this particular field, persuade us that exclusivity is necessary to incentivize investment in this technology. This incentive is especially important in a situation like this one, where commercial interest in the invention has been low and only small companies who are willing to take greater risks can be expected to request a license. The advertised field of use is no greater than necessary and will be narrowed to a few gene-editing targets and specified aptamers upon execution of the follow on Exclusive Commercialization License. The field of use will also be term limited. NCI does not have the commercial expertise nor resources to develop early stage inventions and must rely on the private sector to bring its technologies to the marketplace so that they can be used by the public. In our judgment, this license will tend to increase market competition of drug delivery agents and gene-editing therapeutics, advancing therapeutic options and public health in general, because this is only one of many potentially viable therapeutics that address the indication or use this core technology.

Importantly, additional fields of use covered by the patent claims are still available for licensing. These include methods for hybridizing proteins and imaging agents, which are additional applications that we may be able to license to competent applicants, further increasing competition in the marketplace. NCI intends to continue marketing the technologies by promptly advertising the additional uses to attract additional licensees. The NCI would be happy to send KEI a copy or link to the abstract when published.

With respect to your request for unpublished patent applications, all relevant patent application information for this technology appears to be publicly available and can be found at the USPTO Public Pair or WIPO databases and attached herein for your convenience.

REL0000024364.0001.0001

- E-765-2013:
 - o <http://appft1.uspto.gov/netacgi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20170121708.PG.NR.&OS=DN/20170121708&RS=DN/20170121708>
 - o <https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2015042101>
- E-078-2016:
 - o https://patentscope.wipo.int/search/en/detail.jsf;jsessionid=DCC77A39E9F573EE8B954C152AA85F4F.wapp2nA?docId=WO2017139758&recNum=201&office=&queryString=&prevFilter=%26fq%3DOF%3AWO%26fq%3DICE_M%3A%22C12N%22&sortOption=%E5%85%AC%E5%B8%83%E6%97%A5%E9%99%8D%E5%BA%8F&maxRec=40468

With respect to your comment about the company's employee profiles, the company is a U.S. based startup company incorporated in Delaware. Other companies working in the same space have been directly contacted regarding this matter and have declined to apply for a license to this technology and have submitted no comments objecting to this intent to grant.

The public comment period is now closed. We have considered all your comments and will consider all comments prior to negotiating the proposed license.

Sincerely,

Jasmine Yang, Ph.D.
 Senior Technology Transfer Manager
 NCI Technology Transfer Center

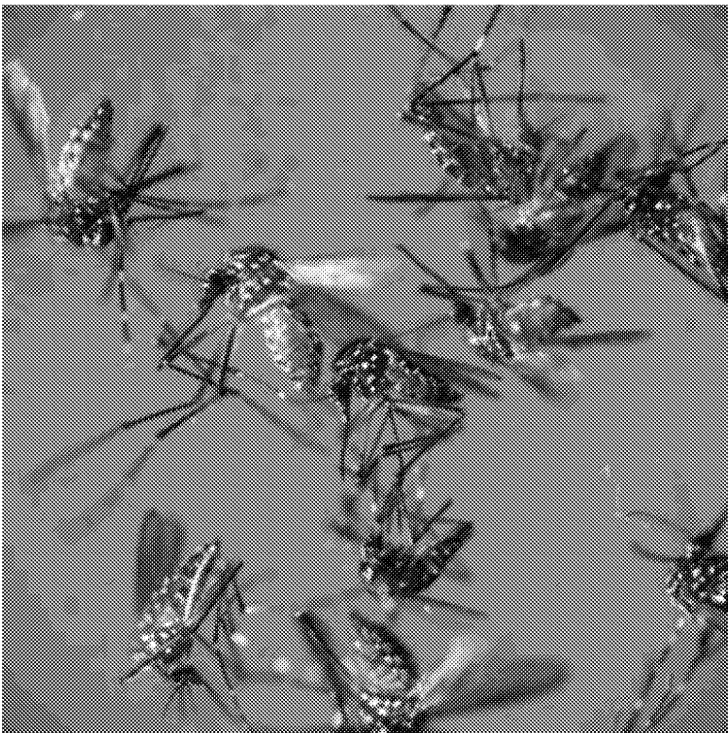
From: Mowatt, Michael (NIH/NIAID) [E] [/O=NIH/OU=NIH/EXCHANGE/CN=NIH/NIAID/CN=MMOWATT]
Sent: 6/27/2017 12:36:50 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: FW: STAT: More lawmakers want the Army to hold a hearing on Zika vaccine pricing

From: Folkers, Greg (NIH/NIAID) [E]
Sent: Monday, June 26, 2017 9:01 PM
Subject: STAT: More lawmakers want the Army to hold a hearing on Zika vaccine pricing

More lawmakers want the Army to hold a hearing on Zika vaccine pricing

By Ed Silverman @Pharmalot

June 26, 2017



Felipe Dana/AP

A half dozen U.S. senators want the U.S. Army to hold a public hearing to explore the controversy over the pricing of a Zika virus vaccine that Sanofi is developing with taxpayer dollars.

In a letter sent on Monday to Acting U.S. Secretary of the Army Robert Speer, the lawmakers expressed concerns that a vaccine would not be “accessible and affordable” for many Americans, since the company may win an exclusive license to develop the technology and have “monopolistic” rights through 2036.

In making their request, the senators noted Sanofi, which is one of the world's largest vaccine makers, has already won a \$43 million government grant and stands to receive another \$130 million to run late-stage trials. Among signing the letter was Sen. Bernie Sanders (I-Vt.), who has been pushing the Army for the last six months to either issue a non-exclusive license or win a pricing commitment from Sanofi.

advertisement

As we reported recently, the company in April rejected a request from the Army to agree to some form of pricing limitations in the U.S., although overall licensing talks are still under way. [UPDATE: An Army spokeswoman wrote us that the Army "is still reviewing the intent of the letter before any determination is made as to the next steps."]

At the same time, the same lawmakers sent a separate letter to Sanofi chief executive Olivier Brandicourt in which they promised they "will continue to urge the Army not to finalize any contracts with your company" until the company agrees to a reasonable and affordable price for a finished vaccine. They also wrote they find it "incomprehensible" Sanofi won't commit to an affordable price.

Lawmakers ask U.S. Army to hold a hearing on Zika vaccine licensing

The senators noted the company would be eligible for a voucher, which can be sold, once any vaccine receives regulatory approval. And they asked the company for information about its research and development spending on Zika vaccines and the amount of funding Sanofi drugs has received from U.S. government entities over the last five years for all of its licensed drugs. We asked Sanofi for comment and will update you accordingly.

This is the second time this month that a group of D.C. lawmakers have asked the Army to hold such a hearing. Two weeks ago, eight House Democrats and one Republican sent a similar letter, although there was no indication from the Army that a hearing would be held. We asked the Army again whether a hearing will now be scheduled and will pass along any reply.

And last month, Louisiana Gov. John Edwards warned Speer that if the mosquito-borne virus spreads, the possibility of monopoly pricing "could cripple state budgets and threaten public health."

These latest missives underscores a growing debate about the extent to which drug makers should be allowed to benefit from products that are developed — at least in part — with taxpayer funds. In this instance, the lawmakers and several consumer advocates are concerned over speculation that, if the virus spreads quickly, Sanofi will have a lock on a potentially lucrative market.

One advocacy group, Knowledge Ecology International, pointed to pricing disparities for Sanofi's Aubagio multiple sclerosis drug. Americans using a coupon can pay about \$6,100 for a month's supply — which is seven times more than patients pay in France and at least four times the price in the U.K., Ireland, and Australia. Sanofi countered that prices vary due to circumstances in each country.

A Sanofi executive recently indicated a price has not been set, but the company intends to price any vaccine in order to "facilitate access" in the interest of public health and is not pursuing the project for a "commercial return." Nonetheless, there is ongoing concern that Sanofi will pursue a similar approach to pricing a Zika vaccine.

[UPDATE: A Sanofi spokeswoman wrote us that “it is in the public-health interest for Sanofi to price this and other vaccines in a way that will facilitate access to and usage of a preventative vaccine. We have demonstrated this commitment in the past, and, if we bring a Zika vaccine to market, we intend to do so for Zika.”]

The controversy has triggered debate over whether the federal government should reinstate language in research agreements that contain “reasonable pricing.” This requirement was removed by the U.S. National Institutes of Health in 1995 over concerns that such clauses would be seen by industry as a “restraint” on new product development.

Contact the Author

Ed Silverman can be reached at ed.silverman@statnews.com

Follow Ed on Twitter [@Pharmalot](https://twitter.com/Pharmalot)

Disclaimer: Any third-party material in this email has been shared under fair use provisions of U.S. copyright law, without further verification of its accuracy/veracity. It does not necessarily represent my views nor those of NIAID, NIH, HHS, or the U.S. government.

From: Allen-Gifford, Patrice (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=67262490D6D441B48EFEC1AFF0700250-ALLENGIFFOR]
Sent: 11/8/2017 1:19:22 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Koeneman, Sandy (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=90529e3e4b02460583239ed3b5b20682-koenemas]
Subject: RE: March In letter sent to HHS in Sept

Thanks Mark.

b5

Patrice

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, November 07, 2017 8:18 PM
To: Allen-Gifford, Patrice (NIH/OD) [E] <patrice.allen-gifford@nih.gov>
Cc: Koeneman, Sandy (NIH/OD) [E] <sandra.koeneman@nih.gov>
Subject: Re: March In letter sent to HHS in Sept

Yes she is aware but no rush. Thx

Sent from my iPhone

On Nov 7, 2017, at 7:44 PM, Allen-Gifford, Patrice (NIH/OD) [E] <patrice.allen-gifford@nih.gov> wrote:

Hi Mark,

I'll ask the team to check if HHS has assigned yet.

b5

b5

We will check though and let you know. Has this letter been raised to Carrie's attention?

Thanks,
Patrice

Patrice Allen-Gifford
Director
Executive Secretariat
301-496-3976

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, November 07, 2017 3:30 PM
To: Allen-Gifford, Patrice (NIH/OD) [E] <patrice.allen-gifford@nih.gov>; Koeneman, Sandy (NIH/OD) [E] <sandra.koeneman@nih.gov>
Subject: March In letter sent to HHS in Sept

Patrice and Sandy:

KEI sent a march-in request for Zinbryta to HHS, no cc to NIH. Since it is NIH funded technology, it should come to the NIH, but I have not seen anything. Have you?
It should be assigned to OSP and OIR.

Here is the letter: <https://www.keionline.org/sites/default/files/KEI-letter-Zinbryta-14Sep2017.pdf>

REL0000024369

Thx

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director
National Institutes of Health

From: Bruff, Susan (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=D3BDF8CAC94049DCAB28D2EB5FAD5137-BRUFFS]
Sent: 10/15/2018 6:01:51 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: Agenda Items

No problem.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, October 15, 2018 1:57 PM
To: Bruff, Susan (NIH/OD) [E] <bruffs@od.nih.gov>
Subject: RE: Agenda Items

If not too late....Oral arguments in KEI v. NIH

From: Bruff, Susan (NIH/OD) [E]
Sent: Monday, October 15, 2018 7:48 AM
To: OD-OSP Senior Staff <ODODPSS@OD.NIH.GOV>
Subject: Agenda Items

Hi all,

Please send me your agenda items for tomorrow's staff meeting by noon today.

Thank you,
Susan

*Susan Bruff
Program Manager
Office of Science Policy
Office of the Director
National Institutes of Health
6705 Rockledge Drive, Suite 750
Bethesda, Maryland 20892
Phone: 301-594-5419
Fax: 301-496-9839*

*Please follow us on Twitter: @CWolinetzNIH
Subscribe to "Under the Poliscopes" NIH OSP's new blog!*

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 5/8/2018 7:15:57 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: Legal/regulatory restrictions on transfers of NIH-funded IP

Or as an alternative,

b5

From: Hammersla, Ann (NIH/OD) [E]
Sent: Tuesday, May 08, 2018 3:15 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: FW: Legal/regulatory restrictions on transfers of NIH-funded IP

After you meet with KEI – let me know.....

From: Myles, Renate (NIH/OD) [E]
Sent: Tuesday, May 08, 2018 3:02 PM
To: Rogers, Karen (NIH/OD) [E] <RogersK@od.nih.gov>
Cc: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: Legal/regulatory restrictions on transfers of NIH-funded IP

Hi all:

OCPL wouldn't respond to KEI for a meeting request they have into OTT. We respond to media requests and public inquiries.

Thanks,
Renate

Renate Myles, MBA
Acting Deputy Director
Office of Communications and Public Liaison
Chief, News Media Branch
National Institutes of Health
Tel: 301-435-3638
Email: mylesr@mail.nih.gov

NIH . . . Turning Discovery Into Health

From: Rogers, Karen (NIH/OD) [E]
Sent: Tuesday, May 08, 2018 2:54 PM
To: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>
Cc: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: FW: Legal/regulatory restrictions on transfers of NIH-funded IP

Hi Renate -- I just spoke with Mark Rohrbaugh and he (and received Ann's e-mail) suggested that

b5

b5

b5

Thanks, Karen

REL0000024373

Karen L. Rogers
Acting Director
Office of Technology Transfer
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, MD 20852
E-Mail: RogersK@nih.gov
Phone: 301-435-4359
Fax: 301-402-8678

SENSITIVE/CONFIDENTIAL INFORMATION

The attached information may be confidential. It is intended only for the addressee(s) identified above. If you are not the addressee(s), or an employee or agent of the addressee(s), please note that any dissemination, distribution, or copying of this communication is strictly prohibited. If you have received this e-mail in error, please destroy the document and notify the sender of the error. Thank you.

From: Hammersla, Ann (NIH/OD) [E]
Sent: Tuesday, May 08, 2018 2:39 PM
To: Rogers, Karen (NIH/OD) [E] <rogersk@od.nih.gov>
Subject: FW: Legal/regulatory restrictions on transfers of NIH-funded IP

Karen: [REDACTED] - Renate Myles. Ann

From: Andrew Goldman <andrew.goldman@keionline.org>
Sent: Tuesday, May 08, 2018 11:28 AM
To: Rogers, Karen (NIH/OD) [E] <RogersK@od.nih.gov>
Cc: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; robert.silverman@oxfam.org; Jamie Love <james.love@keionline.org>
Subject: Re: Legal/regulatory restrictions on transfers of NIH-funded IP

Dear Ms. Rogers: Thank you for your quick reply. We would be interested in discussing both scenarios.

Best,
Andy

--
Andrew S. Goldman
Counsel, Policy and Legal Affairs
Knowledge Ecology International
andrew.goldman@keionline.org // www.twitter.com/ASG_KEI
tel.: +1.202.332.2670
www.keionline.org

On Mon, May 7, 2018 at 4:49 PM, Rogers, Karen (NIH/OD) [E] <rogersk@od.nih.gov> wrote:

Hi Mr. Goldman – My office would not be the appropriate one to discuss this with you. I would like to direct you to the correct staff at the NIH. Can you let me know if the NIH-funded intellectual property was supported through grants or if the technology was developed at the NIH and licensed? Regards, Karen

REL0000024373

Karen L. Rogers

Acting Director

Office of Technology Transfer

National Institutes of Health

6011 Executive Boulevard, Suite 325

Rockville, MD 20852

E-Mail: RogersK@nih.gov

Phone: 301-435-4359

Fax: 301-402-8678

From: Andrew Goldman [mailto:andrew.goldman@keionline.org]

Sent: Monday, May 07, 2018 4:11 PM

To: Rogers, Karen (NIH/OD) [E] <rogersk@od.nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>

Cc: robert.silverman@oxfam.org; Jamie Love <james.love@keionline.org>

Subject: Legal/regulatory restrictions on transfers of NIH-funded IP

Dear Karen, Ann:

I have cc'd Robert Silverman of Oxfam, and James Love of KEI, as we had hoped to have a conversation with you regarding the NIH's authority to restrict offshore transfers of NIH-funded intellectual property from a company to a subsidiary or affiliate.

Would you have time for a phone call on this? If there is a different office in NIH that you think would be more appropriate for this conversation, please let us know.

Kind regards,

REL0000024373

Andrew S. Goldman

Counsel, Policy and Legal Affairs

Knowledge Ecology International

andrew.goldman@keionline.org // www.twitter.com/ASG_KEI

tel.: [+1.202.332.2670](tel:+12023322670)

www.keionline.org

From: Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=HAMMERSLAA]
Sent: 7/10/2017 11:17:13 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Joe Allen [jallen@allen-assoc.com]
Subject: RE: DoD bill language

See references to Xtandi: "Consumer groups have asked the Trump administration to pursue this approach for Xtandi, but have so far no received a reply. ???

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, July 07, 2017 4:53 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Joe Allen <jallen@allen-assoc.com>
Subject: FW: DoD bill language

Subject: RE: DoD bill language

Here's another article on the amendment: <https://www.statnews.com/pharmalot/2017/07/06/xtandi-zika-king-amendment-defense/>. Note that the link for the amendment is to Sen. King's press release, not the actual text.

A proposal would limit prices on meds developed with Defense Department dollars

By ED SILVERMAN @Pharmalot
JULY 6, 2017
AFP/GETTY IMAGES

A U.S. senator is trying to lower prices for medicines that are discovered with taxpayer dollars, and his effort amounts to a new twist to unraveling a complicated controversy that has embroiled the U.S. Department of Defense, large drug makers, numerous lawmakers, and consumer groups. Late last month, Angus King (I-Maine) successfully added an amendment to a Defense Department funding bill that consumer groups say would effectively allow an end run around drug makers that priced products — which were developed with taxpayer dollars — higher than what is charged in seven other countries. The trigger would be determined by median prices and per capita income compared with the U.S.

The move comes amid heightened debate over the extent to which companies should be permitted to profit from medical inventions that are funded — at least, in part — with U.S. taxpayer dollars.

One example is the Xtandi prostate cancer drug, which was originally invented at the University of California, Los Angeles, with grants from the National Institutes of Health and the Department of Defense. One of the chief inventors was a professor at UCLA, which then licensed the drug to Medivation. That company then struck a marketing deal with Astellas, and Medivation was later acquired by Pfizer.

The drug has an average wholesale price in the U.S. of more than \$129,000, about two to four times more than what other high-income countries are paying, according to the Union for Affordable Cancer Treatment and Knowledge Ecology International. The groups have pointed out that Medicare paid more than \$790 million in 2015, up from \$447 million in 2014, and the pricing led to high co-payments.

Meanwhile, the U.S. Army may offer an exclusive license for a Zika virus vaccine to Sanofi. A growing number of lawmakers are concerned that a vaccine would not be accessible or affordable for many Americans, since the company would have monopoly rights through 2036. Lawmakers want the Army to offer a non-exclusive license after Sanofi rejected an Army request to offer a pricing commitment.

Some lawmakers and consumer groups have tried various tactics to win assurances for taxpayers that these products will be accessible, but have so far met with little success. The amendment offered by King, which a spokeswoman explained will not become available until next week, appears to be the first such effort to tie Defense Department funding to prices of medicines that were developed with taxpayer dollars.

In a statement issued late last month, King's office said "the provision directs the Department of Defense to authorize third parties to use inventions that benefited from department funding whenever the price of a drug, vaccine, or other medical technology is higher in the U.S. than the median price charged in the seven largest economies that have a per capita income at least half the per capita income of the U.S."

"Senator King's amendment would protect U.S. residents from paying more than everyone else for drugs based upon inventions when the Department of Defense funded the R&D," said Jamie Love of KEI. "To put it in very non-technical terms, the bottom line is the government would break a monopoly if a company was screwing Americans."

Love believes the amendment would allow the federal government to issue so-called march-in rights, which refer to overriding a patent. Under federal law, this allows an agency that funds private research to require a drug maker to license its patent to another party in order to "alleviate health and safety needs which are not being reasonably satisfied" or when the benefits of a drug are not available on "reasonable terms."

Consumer groups have asked the Trump administration to pursue this approach for Xtandi, but have so far not received a reply. The same request was made to the Obama administration, but the National Institutes of Health, which the groups had petitioned, rejected the request.

A spokeswoman for the Pharmaceutical Research & Manufacturers of America, the industry trade group, wrote us that the amendment "ignores the subsequent substantial R&D investments and risks undertaken by the private sector in developing and bringing a new medicine to patients. This

amendment would undermine critical intellectual property rights and incentives, create substantial uncertainty for companies, and establish completely arbitrary criteria for taking intellectual property. This could chill critically needed collaborations and investment by the private sector to address some of our most serious unmet medical needs.”

Spokespeople for Astellas and Pfizer declined comment. We asked Sanofi for comment and will update you accordingly.

Meanwhile, several congressional lawmakers recently wrote to Sanofi, saying they would urge the Army not to finalize any contracts with the drug makers unless a deal was reached to provide a reasonable and affordable price for a finished Zika vaccine. Other lawmakers have asked the Army to hold a hearing on its licensing process and negotiations with Sanofi, but the Army has not indicated if it will do so.

A Sanofi executive recently indicated a price has not been set, but the company intends to price any vaccine in order to “facilitate access” in the interest of public health and is not pursuing the project for a “commercial return.” Another executive previously indicated that royalties would be paid, but details have not been released as negotiations continue.

Contact the Author

Ed Silverman can be reached at ed.silverman@statnews.com
Follow Ed on Twitter [@Pharmalot](https://twitter.com/Pharmalot)

From: Jambou, Robert (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=FF42A9FA39824980AA9E36AF49E56CBC-JAMBOUR]
Sent: 7/26/2018 10:02:53 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: KEI [Goldman] FOIA #45260
Attachments: RE_KEI [Goldman] FOIA #45260_mrEdits.pdf

Hi Mark,

Thanks for the quick turn-around.

I have incorporated your suggestions for redactions / withholding into the list of records (everything highlighted yellow or green in the attached). The orange highlights indicate changes such as removing a record because it is not responsive or a flat-out full denial has been requested. You can read my comments in the attached.

I did not understand the following:

b5

Bob J.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, July 25, 2018 6:49 PM
To: Jambou, Robert (NIH/OD) [E] <jambour@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

b5

b5

From: Jambou, Robert (NIH/OD) [E]
Sent: Monday, July 23, 2018 12:49 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

Done — I added the incoming request to the TTIP FOIA folder — see page 2 (blue highlight).

Bob J.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 23, 2018 12:36 PM
To: Jambou, Robert (NIH/OD) [E] <jambour@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

Will do. Can you remind me what the request was exactly?

From: Jambou, Robert (NIH/OD) [E]
Sent: Monday, July 23, 2018 12:32 PM

REL0000024378

To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>

Subject: KEI [Goldman] FOIA #45260

Hi Mark,

I have finished the review of the KEI March-In Petition FOIA.

There are 322* responsive .pdf files (including attachments) for your QC review.

To facilitate the task, I have divided the responsive categories into 3 types:

b5

If you could take a look at these files, I would appreciate it (especially the ones labeled "Check or muCheck". If you have comments, please use the Adobe comment tool and add your initials to the end of the file so I can spot those quickly.

I have created a folder and copied the responsive files here into three different sub-folders according to status: <I:\TTIP\KEI Goldman FOIA 45260>

Happy to help you with this. Let me know

Couple important points:

b5

Regards,

Bob J.

REL0000024378

From: Rohrbaugh, Mark (NIH/OD) [E]
To: Jambou, Robert (NIH/OD) [E]
Subject: RE: KEI [Goldman] FOIA #45260
Date: Wednesday, July 25, 2018 6:49:03 PM

b5

b5

From: Jambou, Robert (NIH/OD) [E]
Sent: Monday, July 23, 2018 12:49 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

Done – I added the incoming request to the TTIP FOIA folder – see page 2 (blue highlight).

Bob J.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 23, 2018 12:36 PM
To: Jambou, Robert (NIH/OD) [E] <jambour@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

Will do. Can you remind me what the request was exactly?

From: Jambou, Robert (NIH/OD) [E]
Sent: Monday, July 23, 2018 12:32 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: KEI [Goldman] FOIA #45260

Hi Mark,

I have finished the review of the KEI March-In Petition FOIA.

There are 322* responsive .pdf files (including attachments) for your QC review.

To facilitate the task, I have divided the responsive categories into 3 types:

b5

If you could take a look at these files, I would appreciate it (especially the ones labeled "Check or muCheck". If you have comments, please use the Adobe comment tool and add your initials to the end of the file so I can spot those quickly.

I have created a folder and copied the responsive files here into three different sub-folders according to status: [I:\TTIP\KEI_Goldman_FOIA_45260](#)

Happy to help you with this. Let me know

Couple important points:

b5

Regards,

Bob J.

From: Stevens, Ashley J [astevens@bu.edu]
Sent: 10/26/2016 3:30:19 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: Publishing the updated drug study

I'm going to write the article that I discussed below. It's too bad that you can't be a co-author.

b4

Best regards,

Ashley

Ashley J. Stevens D.Phil. (Oxon), CLP
President
Focus IP Group, LLC

Office: (781) 721-2670
Cell: **b6**
astevens@fipgllc.com

From: Rohrbaugh, Mark (NIH/OD) [E] [mailto:RohrBauM@od.nih.gov]
Sent: Tuesday, October 25, 2016 10:18 AM
To: Stevens, Ashley J
Subject: Re: Publishing the updated drug study

Ok when I get back from b6 next week.

b4

Sent from my iPhone

On Oct 25, 2016, at 2:50 PM, Stevens, Ashley J <astevens@bu.edu> wrote:

The story of Gleevec is in one of the two books on it – are you aware of them? I can give you some dirt.

b4

Best regards,

Ashley

Ashley J. Stevens D.Phil. (Oxon), CLP
President
Focus IP Group, LLC

Office: (781) 721-2670
Cell: b6
astevens@fipgllc.com

From: Rohrbaugh, Mark (NIH/OD) [E] [<mailto:RohrBauM@od.nih.gov>]

Sent: Tuesday, October 25, 2016 5:15 AM

To: Stevens, Ashley J

Cc: Fred Reinhart (fred@research.umass.edu)

Subject: Re: Publishing the updated drug study

Ashley:

My office is working on a paper on kinase inhibitors starting with Gleevec as a breakthrough. Not focused on source of molecules.

b4

Regards,
Mark

Sent from my iPhone

On Oct 25, 2016, at 9:19 AM, Stevens, Ashley J <astevens@bu.edu> wrote:

b4

Best regards,

Ashley

Ashley J. Stevens, D.Phil(Oxon), CLP, RTTP

<image001.jpg>

President

70 Yale Street, Suite 100

Winchester, MA 01890-2331

Tel: (781) 721-2670

Cell: b6

astevens@fipgllc.com

From: Wojtowicz, Emma (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=WOJTOWICZEME6D]
Sent: 8/29/2016 6:32:33 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHExchange/cn=OD/cn=ROHRBAUM]
CC: Myles, Renate (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=recipients/cn=mylesr]; Fine, Amanda (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Fineab]
Subject: FW: Canadian media question?
Attachments: Xtandi-March-In-Request-Letter-14Jan2016.pdf; Biolyse letter re enzalutamide.pdf; Final-Response-NIH june 2016.pdf

Hi Mark-

We received an inquiry from the Canadian Broadcasting Corporation about march-in rights and Xtandi. We wanted to run our response by you to see if anything has changed since June. Please let us know if you have any edits or concerns.

Response:

b5

Thank you-
Emma

From: Kelly Crowe [mailto:kelly.crowe@cbc.ca]
Sent: Monday, August 29, 2016 1:52 PM
To: Myles, Renate (NIH/OD) [E] <mylesr@od.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: Canadian media question?

Hello

My name is Kelly Crowe and I am a medical sciences correspondent with the Canadian Broadcasting Corporation, National News, in Toronto.

I am writing to ask for a comment from the NIH about an offer by a Canadian pharmaceutical company, Biolyse Pharma Corporation, to manufacture the prostate cancer drug Xtandi (enzalutamide) at a reduce price.

I have attached the letter Biolyse wrote to Dr. Frances Collins, in April. I would also appreciate a comment on the NIH response to Knowledge Ecology International, which petitioned the NIH to exercise its march-in rights, or royalty-free rights on enzalutamide. I have attached the letter to the NIH director from Andrew Goldman, along with Dr. Collins' response.

My question concerns the NIH decision to decline the opportunity to have the drug manufactured and supplied at a more affordable price. Why did the NIH turn down this opportunity? Has the NIH ever exercised its

march-in or royalty-free rights on any drug? Is the NIH reconsidering the offer from Biolyse, or the petition from Knowledge Ecology International?

I am filing a story tomorrow on the Canadian company's offer to make the drug at a more affordable price, and I would appreciate a comment from the NIH about their offer, and about Knowledge Ecology International's petition.

I appreciate any assistance you can offer.

Thank you

Kelly Crowe
Medical Sciences Correspondent
CBC National News
416-205-2539 (desk)
b6 (cell)



January 14, 2016

The Honorable Sylvia Mary Mathews Burwell
Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201
Via: Sylvia.Burwell@hhs.gov

Francis Collins, M.D., Ph.D.
Director
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892
Via: Francis.Collins@nih.hhs.gov

The Honorable Ashton Carter
Secretary
Department of Defense
1400 Defense Pentagon
Washington, D.C. 20301-1400
Via: ashton.b.carter.civ@mail.mil; whs.pentagon.esd.mbx.cmd-correspondence@mail.mil

Dear Secretaries Burwell and Carter and Director Collins:

Introduction

Knowledge Ecology International is a non-profit organization with offices in Washington, DC and Geneva, Switzerland. The Union for Affordable Cancer Treatment (UACT) is a non-profit cancer patient group. More about each group is available on their respective web pages: <http://keionline.org> and <http://cancerunion.org>.

This letter is a request that the U.S. federal government use its rights in patents for the prostate cancer drug (enzalutamide), marketed under the brand name of Xtandi by Japan-based Astellas

Pharma. This is a product that has an average wholesale price (AWP) of \$129,269 per year,¹ and which is far more expensive in the United States than in other countries.

Specifically, we ask the Department of Health and Human Services (DHHS), National Institutes of Health (NIH), and/or the Department of Defense (DoD) to use its royalty-free rights in the relevant patents, or to grant this request for march-in rights. The relevant patents include, but are not limited to, the three patents listed in the FDA Orange Book for Xtandi (7709517, 8183274, and 9126941), all of which were granted to the Regents of the University of California, a public institution. All three inventions were made with the support of the United States government under National Institutes of Health SPORE grant number 5 P50 CA092131 and Department of Defense (Army) grant number W81XWH-04-1-0129.

The statutory basis for the request includes 35 U.S.C. § 202(c)(4), for the royalty-free rights in the patents, and 35 U.S.C. § 203(a)(1-3), noting that the term “practical application” of an invention in 35 U.S.C. § 203(a)(1) is defined by 35 U.S.C. § 201(f) to require that the benefits of an invention are “available to the public on reasonable terms.” It is our contention that the pricing of Xtandi is excessive and discriminatory as regards U.S. citizens.

Xtandi is an expensive drug everywhere, indeed so expensive that access is extremely limited in many countries. But, based upon our research, the prices in the United States are far higher than any other country in the world, despite the fact that the critical research benefited from U.S. taxpayer funded grants from the NIH and DoD.

More generally, we ask the U.S. federal government to adopt the policy that the federal government will use its royalty free rights, or grant licenses under federal march-in rights, when prices in the United States are excessive, and/or higher than they are in high income foreign countries, and to apply that policy in this case for patents on enzalutamide.

Such an approach would be in accord with the policy and objective of the Bayh-Dole Act as stated in 35 U.S.C. § 200, to “protect the public against nonuse **and** the unreasonable use of inventions...” [emphasis added].

The analysis in this document includes the following topics and tables.

1. Prices for Xtandi are much higher in the United States than in other high income countries,
2. The high prices for Xtandi create hardships on U.S. patients,
3. The cost of Xtandi to Medicare,
4. Astellas and Medivation projections of Xtandi sales,
5. The role of the U.S. government in funding research on Xtandi,
6. Enzalutamide is an important cancer drug,

¹ \$88.48 per 40 mg unit, four times a day, 365.25 days per year.

7. The University of California at Los Angeles (UCLA) interest in the patents,
8. Orange Book patent claims for Xtandi,
9. Non-patent exclusivity,
10. Generic supply,
11. Xtandi R&D investments through the 2012 approval for the lead indication,
12. Clinical trials on enzalutamide, including trials subsequent to 2012 NDA,
13. Licensing terms, including reasonable royalty,
14. Funding of research to further develop enzalutamide,
15. Standard for determining the Xtandi prices are unreasonable.
16. Conclusion

Tables:

Table 1.1: Prices for Xtandi 40mg capsule/tabs, in the United States and 13 high income countries.

Table 2.1: Prior authorization requirements and formulary tiers for seven insurers providing reimbursements for Xtandi/enzalutamide

Table 3.1: Xtandi/Enzalutamide/Medicare Part D, 2012 to 2014

Table 4.1: Actual and projected Xtandi sales, FY2013 to FY2015

Table 4.2: Actual Xtandi sales, U.S., 2012 to 2014

Table 8.1: Xtandi Patents

Table 11.1: Trials Reported in FDA Medical Review for 2012 Approval for Xtandi

Table 11.2: Trial enrollment cited in in FDA medical reviews for lead indication of new drugs, 2010 to 2014

Table 11.3: R&D expenditures on Xtandi, 2005-2012 (in thousands of USD)

Table 11.4: R&D expenditures on Xtandi, 2013 and 2014 (in thousands of USD)

Table 12.1: Number of trials funded by Industry, NIH, other "U.S. Fed" and "Other," as reported in ClinicalTrials.Gov, January 6, 2016.

Table 12.2: Number of trials funded by Astellas and/or Medivation, as reported in ClinicalTrials.Gov, January 6, 2016.

Table 15.1: US Average Wholesale Price, relative to prices in reference countries

1. Prices for Xtandi are much higher in the United States than in other high income countries.

Xtandi is sold in 40 mg capsules or tablets, and is prescribed for daily use for as long as the drug continues to be effective and tolerated. The typical dose of Xtandi for the treatment of prostate cancer is 4 x 40 mg per day.

The U.S. average wholesale price (AWP), according to *Redbook* data published April 2015, was \$88.48 per 40 milligram capsule, which amounts to \$353.92 per day, or \$129,269.28 per year (365.25 day year). The average price for Medicare in 2014 was \$69.41 per capsule,² or \$101,408.01 for a full year's treatment.

Astellas Pharma, a Japanese-owned drug company, is exploiting the weak response of the United States to excessive pricing of drugs, and is charging U.S. consumers and third-party payers roughly two to four times as much as the prices in other high income countries. For example, in Norway, a country with a per capita income of \$103,630 in 2014, the price is \$32.43 per 40 mg capsule, just 47 percent of the US Medicare price, and 39 percent of the Redbook AWP for the U.S. private sector.

In Australia, the price is \$23.46 per capsule, roughly one third of the U.S. Medicare price. In Quebec, Canada, the price is \$20.12 per capsule, just 29 percent of the U.S. Medicare price, and 24 percent of the U.S. AWP.

Astellas Pharma, the company that holds the rights to market Xtandi, is a member of the Japan-based Mitsubishi UFJ Financial Group (MUFG) keiretsu. Note that in Japan, the price per 40 mg unit of this UCLA-invented drug is \$26.37, less than one-third of the U.S. AWP.

In our opinion, it is unreasonable, and indeed outrageous, that prices are higher in the United States than in foreign countries, for a drug invented at UCLA using federal government grants.

² See Centers for Medicare and Medicaid Services Medicare Drug Spending Dashboard, available at: https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Dashboard/Medicare-Drug-Spending/Drug_Spending_Dashboard.html

Table 1.1: Prices for Xtandi 40mg capsule/tabs, in the United States and 13 high income countries.

Country	Price per unit, national currency		EX Rate (Jan. 6, 2016)	Price per unit, USD	Percent of 2015 AWP	2014, GNI Per Capita, Atlas Method, USD
USA, April 2015 AWP	88.48	USD	1	\$88.48	100%	\$55,200
USA, 2014 Medicare	69.41	USD	1	\$69.41	78%	\$55,200
Australia	33.04	AUD	0.71	\$23.46	27%	\$64,540
Belgium	29.15	EUR	1.08	\$31.48	36%	\$47,260
Canada, Quebec	28.35	CAN	0.71	\$20.12	23%	\$51,630
France	24.75	EUR	1.08	\$26.73	30%	\$42,960
Germany, public insurance	34.19	EUR	1.08	\$36.93	42%	\$47,640
Italy, procurement price	24.08	EUR	1.08	\$26.01	29%	\$34,270
Japan	3,138.80	Yen	0.0084	\$26.37	30%	\$42,000
The Netherlands	29.15	EUR	1.08	\$31.48	36%	\$51,890
Norway	294.78	NOK	0.11	\$32.43	37%	\$103,630
Spain	29.98	EUR	1.08	\$32.38	37%	\$29,440
Sweden	224.705	SEK	.12	\$26.96	30%	\$61,610
Switzerland	35.82	CHF	0.99	\$35.46	40%	\$88,120*
UK	24.42	GBP	1.46	\$35.65	40%	\$43,430

*Only 2013 was available for Switzerland.

2. The high prices for Xtandi create hardships on U.S. patients.

Recent clinical studies indicate that treatment delays may be harmful to patients. While the drug is relatively new, clinicians are now recommending that doctors prescribe Xtandi before prescribing other drugs that target the same androgen axis, to prevent the development of drug resistance.

Since 2014, the FDA has expanded the use of Xtandi to first line treatment for metastatic castration-resistant prostate cancer (mCRPC) based on the phase III PREVAIL clinical trial. Currently Xtandi (FDA approved, 2012), Zytiga (FDA approved, 2011), and Taxotere (FDA approved, 2004) are the top three prescribed drugs in first line metastatic CRPC treatment.³ However, using Taxotere before Xtandi has been shown to decrease the effectiveness of Xtandi

³ Flaig TW *et al.* Treatment evolution for metastatic castration-resistant prostate cancer with recent introduction of novel agents: retrospective analysis of real-world data. *Cancer Med.* 2015 Dec 29.

by a median overall survival of 15.8 months.⁴ Zytiga and Xtandi are both oral therapeutics that target the androgen signaling axis, and although prospective head-to-head comparison clinical trials are still ongoing, retrospective analysis data have indicated that there is a clear clinical cross-resistance between the two drugs.⁵ In fact, in a study conducted by Schrader *et al.*, it was reported that 48.6% of patients who previously took Zytiga and Taxotere were completely resistant to Xtandi.⁶ Based on the susceptibilities of individual patients, oncologists may want to prescribe Xtandi over Zytiga for its toxicity profile or to patients who cannot tolerate low-dose steroids.⁶ If insurance companies were to restrict the use of Xtandi in favor of Zytiga or Taxotere, it would likely prove detrimental to the survival of those patients.

As a direct result of the high price charged by Astellas, U.S. insurance companies and other third party payers have predictably restricted access to Xtandi. Insurers discourage prescribers by requiring restrictive prior authorizations that prevent use of Xtandi before a patient has failed other treatments. UnitedHealthcare, for example, noted in a memorandum that “Supply limits and/or Step Therapy may be in place.”⁷

Table 2.1 shows information from insurance formularies from across the United States, including whether prior authorization is required and what tier the insurer has placed the drug on in their formulary. Higher tiers generally indicate higher copays and restricted access, and insurers generally use 3- or 5-tier systems. (See the next section for a discussion of Medicare spending on Xtandi.)

Table 2.1: Prior authorization requirements and formulary tiers for seven insurers providing reimbursements for Xtandi/enzalutamide.

Payer	Formulary	Tier	Prior Authorization
Rocky Mountain Health Plans	Good Health Formulary ⁸	3	Yes
Kaiser Permanente	Exchange Formulary ⁹	4	No
Aetna	Three Tier Open Individual Formulary ¹⁰	3	Yes: step therapy
Cigna	Prescription Drug List ¹¹	5	Yes

⁴ Crawford ED *et al.* Treating Patients with Metastatic Castration Resistant Prostate Cancer: A Comprehensive Review of Available Therapies. J Urol. 2015 Dec;194(6):1537-47.

⁵ Zhang T. *et al.* Enzalutamide versus abiraterone acetate for the treatment of men with metastatic castration-resistant prostate cancer. Expert Opin Pharmacother. 2015 Mar;16(4):473-85.

⁶ Schrader AJ *et al.* Enzalutamide in castration-resistant prostate cancer patients progressing after docetaxel and abiraterone. Eur Urol. 2014 Jan;65(1):30-6.

⁷ <https://goo.gl/PFtBkf>

⁸ http://www.rmhp.org/docs/default-source/resources/good_health_formulary.pdf?sfvrsn=10

⁹ https://healthy.kaiserpermanente.org/static/health/pdfs/formulary/mid/mid_exchange_formulary.pdf

¹⁰ <https://goo.gl/Z31uvf>

¹¹ <http://www.cigna.com/individuals-families/prescription-drug-list?consumerID=cigna&indicator=IFP>

BlueCross BlueShield	Federal Employee Program ¹²	4	Yes
Montana Health CO-OP	2015 CoventryOne Prescription Drug List ¹³	4	Yes
Anthem BlueCross	Select Drug List 4-Tier Formulary ¹⁴	4	Yes

There is also a racial disparity in the incidence, mortality, and treatment of prostate cancer. NIH and DoD should be concerned that the high price of Xtandi may be contributing to systemic racial discrimination in medical care in the United States. Data collected by the Centers for Disease Control shows that African American men have higher incidence and mortality rates than all other populations. Around two times more African American men have prostate cancer than white men (graph 2.1), and around 2.5 times more African American men die from the disease compared to white men (graph 2.2).¹⁵ In addition, African American men are more likely to have a more aggressive form of prostate cancer. Researchers believe that this racial disparity is the result of sociobiological factors that affect people of African descent.

Beyond sociobiological effects on incidence, mortality, and severity of prostate cancer, African American men face systemic discrimination that affects their access to and quality of treatment. One recent study has found that African-American men on Medicare being treated for nonmetastatic prostate cancer experienced treatment delays, and had more postoperative emergency room visits and readmissions compared to white men.¹⁶ “This might be a form of institutional discrimination based on socioeconomic status resulting in racially disparate outcomes,” wrote Dr. Otis Brawley, chief medical officer of the American Cancer Society, commenting on that study.¹⁷

¹² https://media.fepblue.org/-/media/PDFs/Brochures/FEP_AbbreviatedFormulary_100715.pdf

¹³ <http://www.mhc.coop/wp-content/uploads/docs/MHC-Covered-Drugs.pdf>

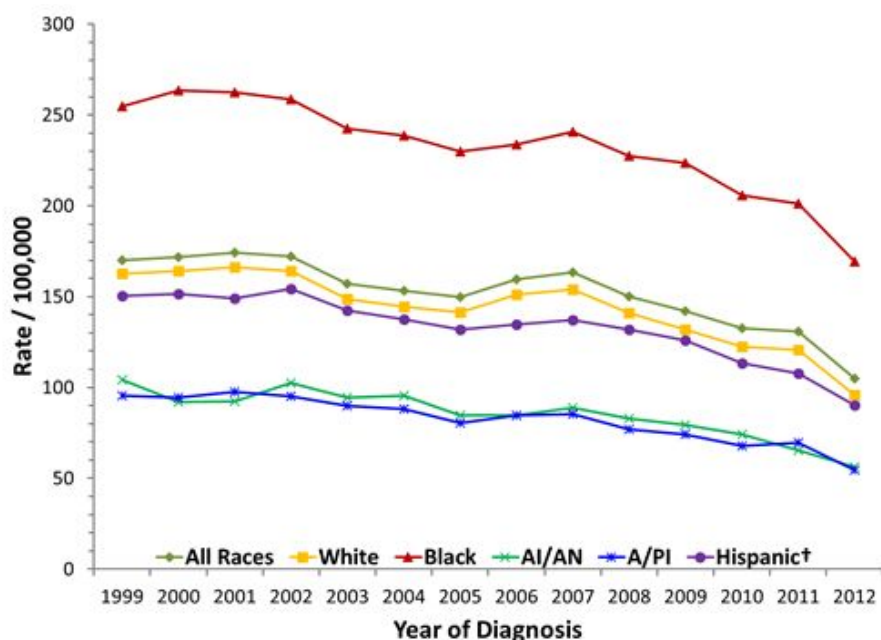
¹⁴ https://fm.formularynavigator.com/MemberPages/pdf/2016CASelectHIX_7006_Full_1576.pdf

¹⁵ See CDC, “Prostate Cancer Rates by Race and Ethnicity,” available at <http://www.cdc.gov/cancer/prostate/statistics/race.htm>.

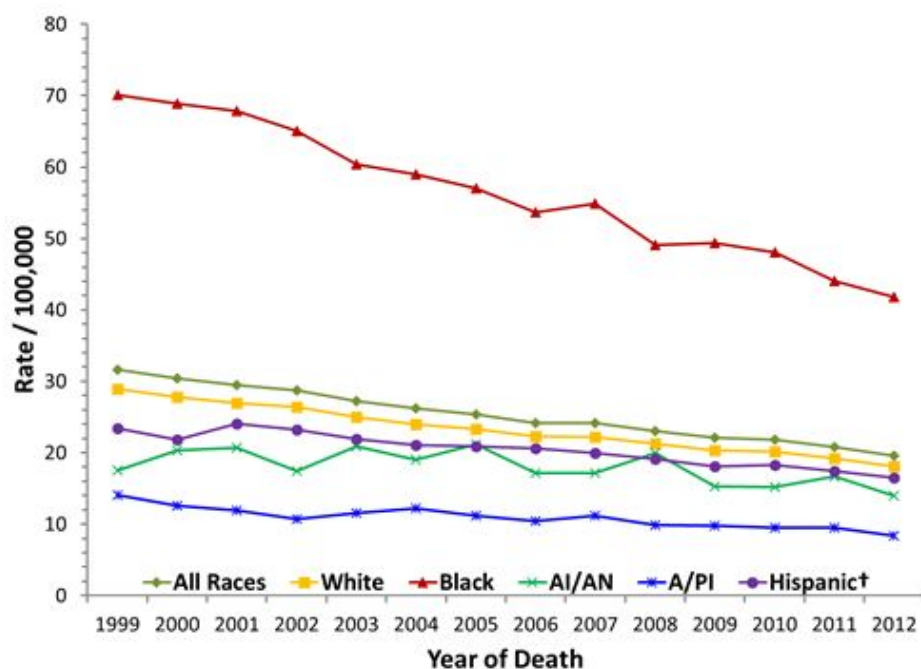
¹⁶ Schmid M et al. Racial differences in the surgical care of Medicare beneficiaries with localized prostate cancer. JAMA Onc. 2015 Oct. doi:10.1001/jamaoncol.2015.3384

¹⁷ Brawley OW. The meaning of race in prostate cancer treatment. JAMA Onc. 2015 Oct. doi:10.1001/jamaoncol.2015.3615

Graph 2.1: “Prostate Cancer Incidence Rates by Race and Ethnicity, U.S., 1999–2012”¹⁸



Graph 2.2: “Prostate Cancer Death Rates by Race and Ethnicity, U.S., 1999–2012”¹⁹



¹⁸ See CDC, “Prostate Cancer Rates by Race and Ethnicity,” available at <http://www.cdc.gov/cancer/prostate/statistics/race.htm>, which contains additional notes on the data/methodologies used to create graphs 1 and 2 in this letter.

¹⁹ See CDC, “Prostate Cancer Rates by Race and Ethnicity,” available at <http://www.cdc.gov/cancer/prostate/statistics/race.htm>.

Veterans who served in Vietnam and the Korean demilitarized zone, who may have been exposed to Agent Orange, are also at higher risk for more aggressive forms of prostate cancer, according to a study conducted by the Department of Veterans Affairs and Oregon Health and Science University.²⁰

3. The cost of Xtandi to Medicare.

According to the Centers for Medicare and Medicaid Services, total Medicare spending on Xtandi grew dramatically from under \$35 million in 2012 to nearly \$447 million in 2014. The increase in outlays from 2013 to 2014 was 93 percent. Part of that growth was due to a 9 percent price increase from 2012 to 2014, a period in which the Consumer Price Index (CPI) grew a mere 3 percent. There was also a steep increase in the number of patients, from 2,143 in 2012, to 7,329 in 2013, and 11,800 in 2014.

Table 3.1: Xtandi/Enzalutamide/Medicare Part D, 2012 to 2014

Year	Total Spending	Beneficiary Cost Share	Beneficiary Count	Total Annual Spending Per User	Avg Cost Per Unit	Claim Count
2012	\$34,898,755.93	\$2,359,870.77	2,143	\$16,285.00	\$63.72	4,519
2013	\$231,503,731.19	\$13,276,790.11	7,329	\$31,587.36	\$64.85	29,572
2014	\$447,311,084.46	\$24,567,059.52	11,800	\$37,907.72	\$69.41	53,980

For prostate cancer, the average age at diagnosis is 66 years. At present, approximately 14 percent of the population is 65 or over, but in five years this will increase to 16 percent, and by 2030 is expected to exceed 19 percent. As the population continues to age, we can reasonably predict that Medicare expenditures on Xtandi will continue to climb.

4. Astellas and Medivation projections of Xtandi sales.

According to the Astellas 2015 annual report,²¹ the United States market will represent 61.16 percent of all global sales of Xtandi, for the fiscal year ending March 31, 2016. Note that in the U.S., sales of Xtandi increased 77 percent from FY2013 (April 1, 2013 to March 31, 2014) to FY2014 (April 1, 2014 to March 31, 2015), and are projected to increase 51 percent from FY2014 to FY2015. This is a steep increase in use for a costly drug.

²⁰ Ansbaugh N et al. Agent Orange as a risk factor for high-grade prostate cancer. Cancer. 2013 Jul; 119(13):2399-2404. Available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4090241/>.

²¹ Astellas Annual Report 2015, available at https://www.astellas.com/en/ir/library/pdf/2015AR_en_1007-2.pdf.

Table 4.1: Actual and projected Xtandi sales, FY2013 to FY2015²²

Country/Region	FY2013	FY2014	FY2015 (projected)
Japan		\$125,147,037	\$193,179,990
U.S.	\$441,000,000	\$779,000,000	\$1,180,000,000
Percent Change in Sales, U.S.		77%	51%
Other Americas	\$8,000,000	\$24,000,000	\$35,000,000
Europe, Middle East, and Africa	\$75,255,950	\$259,095,485	\$505,289,950
Asia/Oceania		\$5,039,478	\$15,958,347
Global	\$524,255,950	\$1,192,282,001	\$1,929,428,288
Percent U.S. Sales to Global	84%	65%	61%

Astellas developed Xtandi in collaboration with Medivation. The Medivation 2015 SEC 10-K filing reports actual Xtandi sales in the United States for calendar years 2012 to 2014.

Medicare's share of sales have increased sharply since 2012. In 2014 they accounted for 66 percent of Xtandi's overall U.S. sales, and 42 percent of global sales. The United States is the largest spender on Xtandi, and most of that money is coming from taxpayers and the insurance payments of aging Americans.

Table 4.2: Actual Xtandi sales, U.S., 2012 to 2014²³

Calendar Year	2012	2013	2014
Xtandi U.S. Sales	\$71,504,000	\$392,415,000	\$679,805,000
Percent Change in U.S. Sales		449% ²⁴	73%
Xtandi Non-U.S. Sales		\$52,800,000 ²⁵	\$381,100,000
Medicare Total Spending	\$34,898,755.93	\$231,503,731.19	\$447,311,084.46
Medicare Share of U.S. Sales	49%	59%	66%
Medicare Share of Global Sales	49%	52%	42%

²² Astellas defines its fiscal year as April 1 to March 31, beginning in the year indicated. Monetary amounts were converted to USD from regional currencies, as necessary.

²³ Medivation 2015 Form 10-K, available at <http://files.shareholder.com/downloads/MDV/1291225255x0xS1193125-15-62576/1011835/filing.pdf>.

²⁴ Note: Xtandi was approved on August 12, 2012, which accounts for low sales.

²⁵ Note: Xtandi was first approved outside the U.S. in June 2013, which accounts for low sales.

5. The role of the U.S. government in funding research on Xtandi.

As noted above, all three patents in the Orange Book for Xtandi disclose the fact that the inventions were made with the support of the United States government under National Institutes of Health SPORE grant number 5 P50 CA092131 and Department of Defense (Army) grant number W81XWH-04-1-0129.

In addition to the grants listed in these three patents, the development of this drug benefited from additional research subsidies from the federal government and charitable foundations, including grants for clinical testing of the drug. For example, a 2009 paper in *Science* reporting on the development of MDV3100 (the development name for enzalutamide)²⁶ acknowledged funding from the Prostate Cancer Foundation, the National Cancer Institute, the DOD PC051382 Prostate Cancer Research Program Clinical Consortium Award, and support from the Charles H. Revson Foundation. Likewise, a 2010 paper in *the Lancet* reporting on a critical Phase 1-2 trial acknowledges the financial support of Medivation, but also the Prostate Cancer Foundation, National Cancer Institute, the Howard Hughes Medical Institute, Doris Duke Charitable Foundation, and Department of Defense Prostate Cancer Clinical Trials Consortium.

27

6. Enzalutamide is an important cancer drug.

In the United States today there are nearly 3 million men suffering from prostate cancer, with over 220,000 new cases in 2015 alone, and 27,540 deaths. It is the third most common form of cancer in the U.S.

When patients are treated early and tumors are localized, the prognosis is often favorable. However, some patients will relapse, leading in nearly all cases to castration resistant prostate cancer (CRPC). At the CRPC stage, the disease is no longer responsive to androgen deprivation therapy (ADT), thus limiting the available treatment options with a greater disease burden. Access to Xtandi/enzalutamide, a non-steroidal second generation androgen receptor agonist, becomes critical to extending the life of the patient, and allowing patients to live an improved quality of life.

There are currently six treatments being used to treat CRPC. Xtandi/enzalutamide has several advantages over the other treatments. Four of the treatments are invasive and require I.V. administration, leukapheresis, or the use of radiopharmaceuticals. Xtandi/enzalutamide and Zytiga are the only daily oral tablets. However Xtandi/enzalutamide's pill burden is lighter since

²⁶ Tran C *et al.* Development of a second-generation antiandrogen for treatment of advanced prostate cancer. *Science*. 2009. May. 8;324(5928):787-90.

²⁷ Scher HI *et al.* Antitumour activity of MDV3100 in castration-resistant prostate cancer: a phase 1-2 study, *Lancet*. 2010 Apr 24;375(9724):1437-46. doi: 10.1016/S0140-6736(10)60172-9.

it does not need to be taken in combination with prednisone. As such, Xtandi/enzalutamide is well tolerated and has more favorable toxicity profile.

Quality of life was also more frequently improved and median time to deterioration was significantly longer with Xtandi/enzalutamide compared to placebo, as reported by patients in functional assessment questionnaires administered during clinical trials.²⁸

With recent and ongoing clinical trials reporting better prostate cancer control when Xtandi/enzalutamide is used in chemotherapy naive CRPC cases or in combination with other agents, it is expected that this drug will soon be prescribed to wider subset of patients.^{29,30,31} In fact experts say that in the next 3 years all CRPC will progress to Xtandi or Zytiga.³²

Xtandi/enzalutamide is also being tested for other types of cancer, including clinical trials for breast cancer (triple negative³³, her2+³⁴), hepatocellular carcinoma³⁵, bladder cancer³⁶, ovarian or fallopian tube cancer,³⁷ pancreatic cancer³⁸ and Mantle Cell Lymphoma³⁹.

7. The University of California at Los Angeles (UCLA) interest in the patents

According to the Medivation's 2014 10-K report to the Securities and Exchange Commission (SEC), the University of California at Los Angeles (UCLA) licensed the patents for the drug to Medivation in exchange for an annual payment of \$2.8 million, a 4 percent royalty on global net sales of the drug, and in addition a 10 percent share of Medivation's sublicensing income

²⁸ Rodriguez-Vida A *et al.* Enzalutamide for the treatment of metastatic castration-resistant prostate cancer. *Drug Des Devel Ther.* 2015 Jun 29;9

²⁹ Scher HI *et al.* Increased survival with enzalutamide in prostate cancer after chemotherapy. *N Engl J Med.* 2012 Sep.

³⁰ Loriot Y *et al.* Effect of enzalutamide on health-related quality of life, pain, and skeletal-related events in asymptomatic and minimally symptomatic, chemotherapy-naïve patients with metastatic castration-resistant prostate cancer (PREVAIL): results from a randomised, phase 3 trial. *Lancet Oncol.* 2015 May.

³¹ STRIDE results presented at 2015 American Society of Clinical Oncology annual meeting, [Clinicaltrials.gov:NCT01981122](http://Clinicaltrials.gov/NCT01981122).

³² Zhang T. *et al.* Enzalutamide versus abiraterone acetate for the treatment of men with metastatic castration-resistant prostate cancer. *Expert Opin Pharmacother.* 2015 Mar;16(4):473-85.

³³ NCT01889238.

³⁴ NCT02091960.

³⁵ NCT02528643, NCT02642913. Hepatocellular carcinoma (HCC, also called malignant hepatoma) is the most common type of liver cancer, often secondary to a viral hepatitis infection (hepatitis B or C) or cirrhosis.

³⁶ NCT02605863, NCT02300610.

³⁷ NCT02300610.

³⁸ NCT02138383.

³⁹ NCT02489123. Mantle cell lymphoma (MCL) is a rare, B-cell NHL that most often affects men over the age of 60.

derived from the Astellas Collaboration Agreement.⁴⁰ The Astellas Collaboration Agreement has separate terms for U.S. and non-U.S. sales, as described below:

Medivation 2014 10-K

p.121:

(c) License Agreement with UCLA

Under an August 2005 license agreement with UCLA, the Company's subsidiary Medivation Prostate Therapeutics, Inc. holds an exclusive worldwide license under several UCLA patents and patent applications covering XTANDI and related compounds. Under the Astellas Collaboration Agreement, the Company granted Astellas a sublicense under the patent rights licensed to it by UCLA.

The Company is required to pay UCLA (a) an annual maintenance fee, (b) \$2.8 million in aggregate milestone payments upon achievement of certain development and regulatory milestone events with respect to XTANDI (all of which has been paid as of December 31, 2014), (c) ten percent of all Sublicensing Income, as defined in the agreement, which the Company earns under the Astellas Collaboration Agreement, and (d) a four percent royalty on global net sales of XTANDI, as defined.

--

p.104-105

(c) Collaboration Revenue

Collaboration revenue consists of three components: (a) collaboration revenue related to U.S. XTANDI sales; (b) collaboration revenue related to ex-U.S. XTANDI sales; and (c) collaboration revenue related to upfront and milestone payments.

[...]

Collaboration Revenue Related to U.S. XTANDI Sales

Under the Astellas Collaboration Agreement, Astellas records all U.S. XTANDI sales. The Company and Astellas share equally all pre-tax profits and losses from U.S. XTANDI sales. Subject to certain exceptions, the Company and Astellas also share equally all XTANDI development and commercialization costs attributable to the U.S. market, including cost of goods sold and the royalty on net sales payable to UCLA under the Company's license agreement with UCLA. The primary exceptions to the equal cost sharing are that each party is responsible for its own commercial FTE costs and that development costs supporting marketing approvals in both the United States and either Europe or Japan are borne one-third by the Company and two-thirds by Astellas. The Company recognizes collaboration revenue related to U.S. XTANDI sales in the period in

⁴⁰ UNITED STATES SECURITIES AND EXCHANGE COMMISSION, Form 10-K, For the Fiscal Year Ended December 31, 2014, <http://www.sec.gov/Archives/edgar/data/1011835/000119312515062576/d850483d10k.htm>

which such sales occur. Collaboration revenue related to U.S. XTANDI sales consists of the Company's share of pre-tax profits and losses from U.S. sales, plus reimbursement of the Company's share of reimbursable U.S. development and commercialization costs. The Company's collaboration revenue related to U.S. XTANDI sales in any given period is equal to 50% of U.S. XTANDI net sales as reported by Astellas for the applicable period.

[...]

Collaboration Revenue Related to Ex-U.S. XTANDI Sales

Under the Astellas Collaboration Agreement, Astellas records all ex-U.S. XTANDI sales. Astellas is responsible for all development and commercialization costs for XTANDI outside the United States, including cost of goods sold and the royalty on net sales payable to UCLA under the Company's license agreement with UCLA, and pays the Company a tiered royalty ranging from the low teens to the low twenties on net ex-U.S. XTANDI sales. The Company recognizes collaboration revenue related to ex-U.S. XTANDI sales in the period in which such sales occur. Collaboration revenue related to ex-U.S. XTANDI sales consists of royalties from Astellas on those sales.

[...]

Medivation came to acquire rights to Xtandi from UCLA through an agreement initiated by Dr. Charles L. Sawyers and Dr. Michael E. Jung, researchers at UCLA working on prostate cancer screening techniques and treatments. Dr. Sawyers is an oncologist who currently runs a lab at Memorial Sloan Kettering Cancer Center and serves on the Board of Directors for Novartis.⁴¹ He was a key participant in the development of Gleeevec and Sprycel, and is a recipient of the Lasker Award. Dr. Michael E. Jung is a Distinguished Professor of Chemistry at UCLA, where he runs a lab that conducts research on chemicals related to the treatment of cancer.

Dr. Sawyers approached Medivation through its founder, Dr. David Hung, a former colleague at the University of California, San Francisco. They settled on an agreement that required Dr. Sawyers and Dr. Jung to disclose all molecules related to their prostate cancer research that benefitted from Medivation funding. Dr. Sawyers served on Medivation's Scientific Advisory Board, as did Dr. Jung, receiving \$20,000 and \$400,000 worth of stocks, respectively.

In addition, Dr. Sawyers and Dr. Jung used the fruits of their research to found their own pharmaceutical firm, Aragon Pharmaceuticals, which they used as a vehicle to develop a drug with a very similar chemical structure to Xtandi. Medivation sued the doctors, Aragon, and UCLA, over the development of that drug.⁴² According to SEC filings, Medivation and UCLA are now engaged in separate litigation over licensing payments on Xtandi.⁴³

⁴¹ More on Dr. Sawyers is available here:

<http://www.bloomberg.com/research/stocks/private/person.asp?personId=12631592&privcapId=25460204>.

⁴² For an amended complaint, filed February 9, 2012, see here: <https://goo.gl/p3lpnm>.

⁴³ Medivation 2015 10-K SEC filing, available here:

<http://files.shareholder.com/downloads/MDV/1291225255x0xS1193125-15-62576/1011835/filing.pdf>.

8. Orange Book patent claims for Xtandi

As noted above, Astellas has listed three patents in the FDA Orange book for Xtandi sales. These include US patent number 7709517, for both a drug substance and drug product claim, and two additional patents, US patent numbers 8183274 and 9126941.

Table 8.1: Xtandi Patents

Patent Number	7,709,517	8,183,274	9,126,941
Title:	Diarylhydantoin compounds	Treatment of hyperproliferative disorders with diarylhydantoin	Treatment of hyperproliferative disorders with diarylhydantoin compounds
Publication date	May 4, 2010	May 22, 2012	Sep 8, 2015
Filing date	May 15, 2006	Feb 18, 2010	Apr 17, 2012
Priority Date	May 13, 2005	May 13, 2005	May 13, 2005
Inventors	Charles L. Sawyers, Michael E. Jung, Charlie D. Chen, Samedy Ouk, Derek Welsbie, Chris Tran, John Wongvipat, Dongwon Yoo	Charles L. Sawyers, Michael E. Jung, Charlie D. Chen, Samedy Ouk, Chris Tran, John Wongvipat	Charles L. Sawyers, Michael E. Jung, Charlie D. Chen, Samedy Ouk, Chris Tran, John Wongvipat
Original Assignee	The Regents Of The University Of California	The Regents Of The University Of California	The Regents Of The University Of California
Expiration date	Aug 13, 2027	May 15, 2026	May 15, 2026
FDA substance claim	Yes		
FDA product claim	Yes		
FDA use claim code		U - 1281; The treatment of patients with metastatic castration-resistant prostate cancer (CRPC) who have previously	U - 1588, The treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

		received docetaxel. U - 1588, The treatment of patients with metastatic castration-resistant prostate cancer (CRPC).	
Disclosure of US rights in the patent	This invention was made with United States Government support under National Institutes of Health SPORE grant number 5 P50 CA092131 and Department of Defense (Army) grant number W81XWH-04-1-0129. The Government has certain rights in the invention.	This invention was made with United States Government support under National Institutes of Health SPORE grant number 5 P50 CA092131 and Department of Defense (Army) grant number W81XWH-04-1-0129. The Government has certain rights in the invention.	This invention was made with Government support under Grant No. W81XWH-04-1-0129 awarded by the United States Army, Medical Research and Materiel Command; Grant No. CA092131 awarded by the National Institutes of Health. The Government has certain rights in this invention.

9. Non-patent exclusivity.

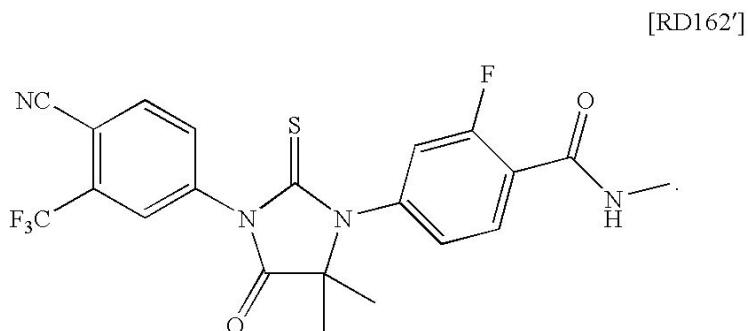
The FDA Orange Book lists two grants of non-patent exclusivity to Astellas for enzalutamide, both expiring in 2017. One was granted for enzalutamide as a new chemical entity, expiring August 31, 2017; the second was granted under code I-693 for “treatment of patients with metastatic castration-resistant prostate cancer (CRPC)”, expiring September 10, 2017. These dates are sufficiently close that they should not be used to excuse non-action on this request, particularly since it may take several months for a generic supplier to prepare data for an Abbreviated New Drug Application (ANDA).

10. Generic supply

Enzalutamide is a small molecule drug that does not have a complex structure.

Enzalutamide is a synthetic, non-steroidal pure antiandrogen, originally named MDV3100, which has the formula $C_{21}H_{16}F_4N_4O_2S$, a molar mass of 464.44 g/mol and a chemical name of 4-(3-(4-Cyano-3-(trifluoromethyl)phenyl)-5,5-dimethyl-4-oxo-2-thioxoimidazolidin-1-yl)-2-fluoro-N-methylbenzamide. The chemical structure, illustrated in Figure 1, includes a thiohydantoin and two benzene groups.

Figure 10.1: Structure of MDV3100 (CAS number: 915087-33-1)



Petitioners have excellent relations with several generic drug manufacturers, and do not anticipate difficulties obtaining the necessary FDA approvals for generic versions of enzalutamide, once the federal government provides access to the patents, either by using the royalty-free right in the patents or granting this march-in request.

Note that the 2015 U.S. AWP for Xtandi of \$88.48 per 40 mg capsule is equivalent to \$2,212 per gram of active pharmaceutical ingredient.

Generic products with similar complexity for manufacturing can be obtained for under \$10 per gram of API, retail,⁴⁴ and considerably less in bulk.

11. Xtandi R&D investments through the 2012 approval for the lead indication

Xtandi was approved as a treatment for prostate cancer in August 31, 2012, as a priority drug under the FDA Priority Review program. The application was by Astellas, and was approved by the FDA as NDA 203415.

The application for the NDA was supported by evidence from four clinical trials, including one Phase 1 trial with 140 patients enrolled, one Phase 1/2 trial with 27 patients enrolled, one Phase 2 trial with 60 patients enrolled, and one Phase 3 trial with 1,199 patients enrolled. Total enrollment for the 4 trials was 1,426 patients.

⁴⁴ For example, generic versions of the cancer drug imatinib.

Table 11.1: Trials Reported in FDA Medical Review for 2012 Approval for Xtandi

Study Number	NCT Number	Phase	Start- End Date	Enrolled (FDA Review)	Study Sponsor	Federal Funding
S-3100-1-01	NCT00510718	1	7/2007- 1/2010	140	Medivation	NCI, DoD ⁴⁵
CRPC-MDA-1	NCT01091103	2	2/2010- 7/2011	60	Medivation	NCI, DoD ⁴⁶
CRPC2	NCT00974311	3	9/2009- 9/2011	1199	Medivation	n/a
9785-CL-0111	NCT01284920	1/2	11/2010- 7/2012	27	Astellas Pharma	n/a

The two earliest trials (NCT00510718, NCT01091103) received subsidies from the National Cancer Institute and Department of Defense, in addition to funding from the Prostate Cancer Foundation and other non-profit institutions. After receiving favorable results from the trials subsidized by NCI and DoD, Medivation and Astellas funded two additional trials.

The size of the trials for Xtandi were typical of other cancer drugs approved from 2010 to 2014 for the lead indication as a New Molecular Entity, and much smaller than trials used to approve non-cancer drugs.

Table 11.2: Trial enrollment cited in in FDA medical reviews for lead indication of new drugs, 2010 to 2014

Average for all cancer drugs	1,316
Average for non-Cancer Drugs	4,733
Xtandi	1,426

Medivation reported their direct expenditures and cost-sharing payments from Astellas for collaboration on the development of Xtandi between 2005 and 2012, when the FDA granted Xtandi marketing approval. They defined direct costs as “clinical and preclinical study costs, cost of supplying drug substance and drug product for use in clinical and preclinical studies, contract research organization fees, and other contracted services pertaining to specific clinical and preclinical studies.”⁴⁷ The number reported excludes indirect costs, which include “administrative and support costs.”⁴⁸

Astellas contributed to half of all direct costs for R&D conducted for U.S. drug approval, two-thirds of costs for R&D directed towards trials aimed at both U.S. and non-U.S. use of

⁴⁵ Scher, Howard I., et al. "Antitumour activity of MDV3100 in castration-resistant prostate cancer: a phase 1–2 study." *The Lancet* 375.9724 (2010): 1437-1446.

⁴⁶ Efsthathiou, Eleni, et al. "Molecular characterization of enzalutamide-treated bone metastatic castration-resistant prostate cancer." *European urology* 67.1 (2015): 53-60.

⁴⁷ Medivation 2009 10-K SEC filing, available here:

<http://files.shareholder.com/downloads/MDV/1291225255x0xS1193125-10-57020/1011835/filing.pdf>.

⁴⁸ Ibid. Indirect costs for all drugs combined are available in Medivation SEC filings.

Xtandi, and full development costs for commercialization outside the United States. Based upon the Medivation SEC filings, R&D outlays on Xtandi were \$303 million through the end of the calendar year 2012.

Table 11.3: R&D expenditures on Xtandi, 2005-2012 (in thousands of USD)

SEC 10-K Year	2005	2006	2007	2008	2009	2010	2011	2012
Medivation Direct Costs	\$261	\$3,021	\$2,619	\$8,845	\$27,046	\$23,454	\$42,3350	\$67,086
Development cost-sharing payments from Astellas					\$2,784	\$34,125	\$44,285	\$47,473
Total	\$261	\$3,021	\$2,619	\$8,845	\$29,830	\$57,579	\$86,620	\$114,559
Cumulative Total								\$303,334

Medivation reported outlays of an additional \$285 million in calendar years 2013 and 2014, much of that money aimed at justifying broader use of Xtandi for prostate cancer, but also on testing the drug to treat other types of cancer.

Table 11.4: R&D expenditures on Xtandi, 2013 and 2014 (in thousands of USD)

SEC 10-K Year	2013	2014
Medivation Direct Costs	\$73,076	\$102,669
Development cost-sharing payments from Astella	\$46,594	\$63,479
Total	\$119,670	\$166,148
Cumulative Total		\$285,818

The company outlays on R&D investments were significant, although it is worth noting that the early and most risky trials were small and subsidized by the United States government.

Note that through the end of 2014, representing a little more than two years of reimbursements, Medicare spent \$704 million on Xtandi. Astellas expects a sharp increase in U.S. sales in 2015 and 2016, and the company revenues also include sales from non-Medicare patients in the United States and patients outside of the United States.

12. Clinical trials on enzalutamide, including trials subsequent to 2012 NDA.

Like many cancer drugs, the initial approval of the drug for the lead indication has lead to continued research to determine the best uses of the drugs, both for prostate cancer patients and to test the benefits of using enzalutamide to treat other types of cancer.

As of January 6, 2015, there were 129 trials listed in the ClinicalTrials.Gov database.

The funding of the trials is reported under the categories Industry, U.S. Fed., NIH, and Other, as well as combinations of those categories.

- 54 of the 129 trials were reported as funded by Industry alone.
- Another 31 trials were reported as funded by Industry and some other funder.
- The NIH or other U.S. Federal agencies were reported as funders in whole or in part of 18 trials.
- The category “Other” is quite important, accounting for 29 trials funded exclusively by Other, and another 42 where “Other” is among the funders.

Many of the trials funded by “Other” refer to universities and other non-profit research organizations that receive NIH or other federal agency research grants. “Other” also refers to funding from foreign governments and charities.

Table 12.1: Number of trials funded by Industry, NIH, other “U.S. Fed” and “Other,” as reported in ClinicalTrials.Gov, January 6, 2016.

Funder	Number of Trials
“Industry” only	54
Mixed including “Industry”	31
“Other” only	29
Mixed including “Other”	42
NIH only	3
Mixed including NIH or other “U.S. Fed”	16

Table 12.2: Number of trials funded by Astellas and/or Medivation, as reported in ClinicalTrials.Gov, January 6, 2016.

Funder	Number of Trials
Astellas and/or Medivation as sponsor of industry only funded trials	39
Astellas and/or Medivation as sponsor of mixed funded trials	18

Among the trials funded in whole or in part by “Industry”, the majority, 57, were funded by Astellas and/or Medivation, and of those only for 39 (30 percent of the 129) were they the sole funder of the trials.

Other companies, such as Lilly, Gilead, Roche, Bayer, Sanofi, and smaller companies, were involved in funding 28 trials.

13. Licensing terms, including reasonable royalty.

We are requesting the federal government grant an open license to any generic drug manufacturer.

The federal government has no obligation to pay royalties on the patents when and if it exercises its royalty free rights in the patents.

If the government orders the licensing of the patents under the federal march-in statutes, the terms of the license, including the royalty, have to be “reasonable under the circumstances.”⁴⁹

The issue of the appropriate royalty rate can be briefed and argued when and if the federal government is inclined to exercise march-in rights on the patent.

“Under the circumstances” would include many factors, such as that the facts motivating the granting of the march-in request are related to abuses of the patent rights, including in particular charging an excessive price and discriminating against U.S. consumers.

Rights in test data

Patents are granted for inventions, but as noted above, patents are not the only intellectual property rights associated with drug development.

The FDA provides additional intellectual property rights for investments in clinical trials, including five years of exclusive rights to rely upon data supporting the registration of a new chemical entity, and three years of rights in the data to support new indications on a drug.

The five years of test data exclusivity for Xtandi as a treatment for patients with metastatic castration-resistant prostate cancer (CRPC) will expire on September 10, 2017 in the United States, and later in many other countries. For example, the term of protection for test data is up to 8 years in Japan and Canada, and 11 years in the European Union.⁵⁰ The rights in test data are designed to protect and reward investments in clinical trials, and they operate separately from patent protection. The existence of the test data rights eliminates the need to consider investments in clinical trials when considering the royalty to the patent holder, because those investments are protected by this separate intellectual property right. As regards the

⁴⁹ 35 USC 203(a).

⁵⁰ Comparison of the Non-patent Drug Exclusivities Available in the United States, Canada, Europe and Japan. The International Economic Forum of the Americas. Serge Lapointe, Ph.D. June 14, 2012 <http://forum-americas.org/sites/default/files/documents/20120614-lapointe-pres.pdf>

investments in the U.S. market, it is likely that Astellas will have earned more than \$5 billion from the U.S. market alone, through September 10, 2017, the date of the most relevant test data exclusivity in the United States ends. Astellas will have also earned billions more from sales outside of the United States, where most patients reside.

Average industry royalty rates

According to the IRS, in 2012, the average rate of aggregate royalties (for all patents, know-how, trademarks, etc.⁵¹), reported on corporate income tax returns for the pharmaceutical and medicine manufacturing sector (MINOR CODE 325410) was 6.95 percent.

14. Funding of research to further develop enzalutamide.

One possible argument against any policy that lowers drug prices or shortens the term of a monopoly is that society benefits from the incentive to invest in R&D to find new uses for a drug.

It is possible to address the objective of providing sustainable sources of R&D funding without having high prices or longer monopolies.

On at least two occasions in the past involving NIH funded cancer drugs, and more recently in connection with proposals to create or extend monopolies in various drafts of the 21st Century Cures Act, there have been proposals to have mandates for funding R&D.

In one case, involving a dispute over the term of the monopoly on the cancer drug cisplatin in the early 1980s, there was a proposal that generic firms be obligated to contribute to the costs of ongoing research to determine new uses for the drug, following generic entry. This proposal, made by a generic drug company seeking to end the cisplatin monopoly, led to a compromise whereby Bristol-Myers was allowed to extend the monopoly for five more years, but only after they lowered the price of cisplatin and contributed tens of millions of dollars to independent research through non-profit institutions, at the direction of the NIH. Later, BMS proposed something similar, in an unsuccessful effort to extend data exclusivity on the cancer drug Taxol. In early drafts of the the 21st Century Cures legislation, there were proposals to associate extensions of drug monopolies with obligations to provide money to the NIH, and to make other investments in R&D.

In this case involving Xtandi, the NIH could simultaneously end the Xtandi monopoly and require any generic drug company to make contributions toward follow-on research to explore new and/or better uses of enzalutamide. Such obligations could be a condition of any use of the federal government's royalty free right in the drug, or as a condition of obtaining a march-in license.

⁵¹ The IRS does not provide a definition of royalties. See: <https://www.irs.gov/pub/irs-tege/eotopicd89.pdf>.

Note that there are benefits in having different parties participate in the testing of drugs, including those that do not have conflicts of interest as regards reporting possible negative impact of products, or allowing greater competition in designing better delivery mechanisms or new combination products. Also, in the case of Xtandi, more than half of the trials involving enzalutamide are already funded by entities other than Astellas.

15. Standard for determining that Xtandi prices are unreasonable.

In determining if the prices for Xtandi violate the statutory obligation to make products available to the public on reasonable terms and conditions, the NIH has broad discretion to consider a variety of factors, including the high price of the drug and the fact that the high price leads to restrictions on access and financial hardships on patients. However, in this case, we recommend the NIH address a narrower question, that can be answered clearly, given the robust evidence.

Do the Astellas prices for Xtandi discriminate against consumers in the United States? And, if so, the NIH should approve the March-In request, or use its royalty free rights in the patents, to prevent U.S. residents from paying more for a drug invented on federal grants than residents of other high income countries.

We have obtained prices for Xtandi in the United States and in 13 other high income countries, and this data allows the NIH to determine whether U.S. consumers are being asked to pay more for a drug invented on federal grants than Astellas charges in other high income countries.

One possible comparison to determine if the price is unreasonable is to consider the prices in other industrialized countries outside of the United States that have (1) per capita incomes of at least half that of the United States, (2) have the large economies as measured by the GDP, and (3) are members of the OECD, and to consider the U.S. price to be unreasonable, if the average wholesale price (AWP) in the U.S. is higher than the median price in the reference countries.

We propose using an odd number of countries. The 13 countries that have incomes at least 50 percent of the United States and which have the largest economies include Japan, Germany, France, the UK, Italy, Canada, Australia, Spain, the Netherlands, Switzerland, Sweden, Belgium and Norway.

We have prices for all 13 of the reference countries. None of the prices are higher than \$36.93, and the April 2015 U.S. AWP was \$88.48. It is not a close call: the U.S. prices are discriminatory and are unfair to U.S. residents. Note that the *highest* price of the 13 high income reference countries was less than half (42 percent) of the average wholesale price (AWP) in the United States, the median of the 13 prices reference prices we have obtained is just 36 percent of the US AWP, and the prices in Japan and Canada are 30 percent and 23 percent respectively of US AWP. As a percentage in 2014 per capita income, the U.S. prices are also

far higher than for any of the 13 high income countries. In eight countries, the annual cost of Xtandi is between 47 percent and 97 percent of annual per capita income. In four countries, the annual cost of Xtandi is between 111 percent and 161 percent of per capita income. In the United States, the annual cost of Xtandi is 234 percent of 2014 per capita income.

Table 15.1: US Average Wholesale Price, relative to prices in 13 reference countries

	2014 GDP	2014 annual Per Capita Income	price per 40 mg unit	Annual price (x 4x 365.25) as percent of 2014 per capita income
United States, Average Wholesale price April 2015	\$17,419,000,000,000	\$55,200	\$88.48	234%
Japan	\$4,601,461,206,885	\$42,000	\$26.37	92%
Germany	\$3,868,291,231,824	\$47,640	\$36.93	113%
France	\$2,829,192,039,172	\$42,960	\$26.73	91%
United Kingdom	\$2,988,893,283,565	\$43,430	\$35.65	120%
Italy	\$2,141,161,325,367	\$34,270	\$26.01	111%
Canada	\$1,785,386,649,602	\$51,630	\$20.12	57%
Australia	\$1,454,675,479,666	\$64,540	\$23.46	53%
Spain	\$1,381,342,101,736	\$29,440	\$32.38	161%
Netherlands	\$879,319,321,495	\$51,890	\$31.48	89%
Switzerland	\$701,037,135,966	\$88,120*	\$35.46	59%
Sweden	\$571,090,480,171	\$61,610	\$26.96	64%
Belgium	\$531,546,586,179	\$47,260	\$31.48	97%
Norway	\$499,817,138,323	\$103,630	\$33.09	47%
Median, reference countries			\$31.48	91%
Unweighted average, reference countries			\$29.70	89%

* For Switzerland, only 2013 per capita income was available.

One defense for the high U.S. price for Xtandi would be that the product could not have been developed at a lower price. But given the significant market for this drug, the federal subsidies in both the preclinical and clinical stages, and the fact that prostate cancer is the among the three most common types of cancer,⁵² that defense can be rejected entirely, and certainly going forward, given the billions of dollars in revenue already earned by Astellas.

16. Conclusion

We are requesting the federal government take steps to address the discriminatory and unfair pricing of Xtandi/enzalutamide by Astellas. U.S. residents should not have to pay two to four

⁵² American Cancer Society: Cancer Facts and Figures 2015. Atlanta, Ga: American Cancer Society, 2015.

times as much for a cancer drug than residents of other high income countries, particularly when the drug was invented with the support of federal grants and benefited from other federal research subsidies. The average wholesale price for Xtandi was \$129,269 per year in 2015, and this was more than twice as high as the price in any other high income country in our 13 country survey, and four times as high as the price in Canada. U.S. taxpayers are generous when it comes to financing research programs at the NIH, the U.S. Department of Defense, and in other federal agencies. However, we should not allow the companies that commercialize this research to discriminate and use unfair prices that impose financial hardships on U.S. residents, create access barriers for cancer patients, and make our workforce less competitive in global markets.

There are many areas where current U.S. laws are inadequate to address excessive or unfair prices. This is not one of them. The Bayh-Dole Act was passed with the promise that the federal March-In rights or the federal government royalty-free rights in patents would be available to protect the public from the unreasonable use of patented inventions. This is such a case.

Please contact Andrew S. Goldman, counsel for Policy and Legal Affairs at KEI, about this request. He can be reached at andrew.goldman@keionline.org, or by telephone at +1.202.332.2670.

Sincerely,

James Packard Love, Andrew S. Goldman, Diane Singhroy, Zack Struver, Claire Cassedy and Elizabeth Rajasingh, on behalf of
Knowledge Ecology International
1621 Connecticut Avenue, Suite 500
Washington, DC 20009
<http://keionline.org>

Manon Ress, Michael Davis and Ruth Lopert, on behalf of
Union for Affordable Cancer Treatment (UACT)
<http://cancerunion.org>

Cc:

Army research Laboratory
Domestic Technology Transfer (Patent Licensing, Cooperative R&D Agreements, Test Service Agreements) via ORTA@arl.army.mil

National Institutes of Health
Karen Rogers, via rogersk@mail.nih.gov
Mark L. Rohrbaugh PhD, JD via RohrbauM@mail.nih.gov.

White House, Office of Science and Technology Policy
John P. Holdren, via jholdren@ostp.eop.gov
Tom Kalil, via: tkalil@ostp.eop.gov

Senators Boxer, Brown, Grassley, King Leahy, McCain McCaskill Nelson Sanders, Schumer
Sessions, and Wyden

Representatives Doggett, Schakowsky, Tom Price, Markwayne Mullin, the Congressional
Prostate Cancer Task Force

Andy Slavitt
Acting Administrator for the Centers for Medicare & Medicaid Services (CMS)
Via Email: Andy.Slavitt@cms.hhs.gov

Francis Collins, M.D., Ph.D.
Director
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892
Via: Francis.Collins@nih.hhs.gov

Dear Administrator Slavitt and Director Collins,

I am a private biotechnology consultant representing Biolyse Pharma Corporation in St.Catharines Ontario. I have attached a letter from Bridgitte Kiecken, the President of Biolyse Pharma, offering to supply Medicare and programs with generic versions of enzalutamide, a drug to treat prostate cancer, at \$3 per 40 mg tablet. In 2014, Medicare was paying \$69.41 per tablet for Xtandi, the Astellas version of the drug, so the Biolyse offer involves dramatic savings to the U.S. government.

The federal government has a royalty free right to use the following three patents on this product: 7709517, 8183274 and 9123941. The Biolyse offer is contingent upon the federal government using the royalty free right to obtain less expensive supplies of the drug.

Separately, Biolyse Pharma would be interested in approaching the NIH to use its rights in the patents to supply affordable versions of enzalutamide in developing countries, including South Africa.

I would be interested in talking with your staff about this offer,

Sincerely,

John R. Fulton
BioNiagara
5 Garden Park Blvd.
St.Catharines, Ontario
Canada
L2R-5B8
905.932.7883
Biolyse@Biolyse.com



Corporation
Biolyse Pharma
Corporation

59 Welland Vale Rd., St. Catharines
Ontario Canada L2S 3Y2
Tel: (905) 687-8008
Fax: (905) 687-4923
Toll Free: 1-877-234-1880
E-mail: biolyse@sympatico.ca

Andy Slavitt
Acting Administrator for the Centers for Medicare & Medical Services (CMS)

April, 22nd, 2016

Dear Mr. Slavitt,

Biolyse Pharma is a Canadian company that specializes in the manufacturing as well as the development of sterile oncology drugs.

We are presently writing to express our willingness to supply a generic version of enzalutamide to prostate cancer patients in the United States and in the developing world.

Presently enzalutamide is sold under the name Xtandi by Astella Pharmaceuticals. It is our understanding, that in 2014, prostate cancer patients receiving reimbursement for their medication were paying an excess of \$250 dollars for their daily regime of four tablets of 40mg of enzalutamide. Astella is presently selling in Canada and in other jurisdictions Xtandi for approximately 30% of what it is presently charging in the United States. Biolyse Pharma would be able to supply enzalutamide for approximately \$3.00 USD per tablet.

Medicare has a royalty free right in all three patents in the FDA orange book for enzalutamide. We believe we can have generic versions approved by the FDA in less than three years if CMS is willing to allow Biolyse Pharma to supply the drug using the U.S federal government's worldwide royalty free license.

Sincerely,

Brigitte Kiecken
President



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

To be e-mailed to: andrew.goldman@keionline.org

June 20, 2016

Andrew S. Goldman
Knowledge Ecology International
1621 Connecticut Avenue, Suite 500
Washington, DC 20009

Dear Dr. Goldman:

Thank you for your January 14 letter and your follow-up correspondence to the Department of Health and Human Services, the Department of Defense, and me requesting that each or both federal agencies (1) exercise its march-in authorities found at 35 U.S.C. § 203, or (2) exercise the federal government's non-exclusive royalty-free government use license for Xtandi® (enzalutamide). Based on the information provided in your letter and follow-up correspondence, and information that is publically available, we decline to initiate a march-in investigation or utilize the government's license in the patents.

More specifically, a federal agency that funded an invention has the right, consistent with 35 U.S.C. § 203(a)(1), to grant a license to a third party if "action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time effective steps to achieve practical application of the subject invention in such field of use." Practical application as defined at 35 U.S.C. § 201 is "...to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms."

As set forth in NIH's prior march-in determinations (1997 Cell Pro; 2004 and 2013 Norvir®; 2004 Xalatan®, see www.ott.nih.gov/policies-reports), practical application is evidenced by the "manufacture, practice, and operation" of the invention and the invention's "availability to and use by the public..." Xtandi® is broadly available as a prescription drug. Your letter states that sales of enzalutamide increased 77% from Fiscal Year 2013 to Fiscal Year 2014 and are projected to increase 51% from Fiscal Year 2014 to Fiscal Year 2015 (from your letter, pages 9-10); however, it provides no information and no information was identified from public sources to suggest that enzalutamide is currently or will be in short supply.

In view of the above information presented in your letter and your follow-up correspondence and public information identified by the NIH, we decline to proceed with the government's march-in authorities at this time or utilize the government's license to the patents. Enclosed for your information is the June 7 Department of Health and Human Services response to Representative Doggett on holding a public hearing.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Francis S. Collins", with a stylized flourish at the end.

Francis S. Collins, M.D., Ph.D.
Director

Enclosure

cc: The Honorable Ashton Carter
Secretary of Defense

The Honorable Secretary Burwell
Secretary of Health and Human Services

Union for Affordable Cancer
Treatment (UACT)



THE SECRETARY OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

JUN 07 2016

The Honorable Lloyd Doggett
U.S. House of Representatives
Washington, D.C. 20515

Dear Representative Doggett:

Thank you for your letter of March 28 expressing your and your colleagues' ongoing concerns about the price of Xtandi® (enzalutamide). I can assure you that Dr. Collins and I share your concerns about the rising costs of drugs and the impact these costs have on Americans' access to life-saving treatments.

In your letter, you encourage the National Institutes of Health (NIH) to hold a public hearing on the use of the Bayh-Dole Act march-in authority for the patented inventions funded by the NIH and U.S. Army that cover Xtandi® (enzalutamide). The NIH considers the application of the statutory criteria for march-in very carefully, according to the process outlined in the statute and implementing regulations at 37 CFR 401.6. At this time, NIH believes this process allows the agency to collect sufficient information to consider the petition without a public hearing.

Over the past decade, the NIH has evaluated three prior march-in requests. The NIH's determinations in these cases, which are publicly available at www.ott.nih.gov/policies-reports, demonstrate how the agency evaluates the evidence regarding the statutory conditions that would justify the exercise of its march-in authority.

The Department of Health and Human Services' goal is to foster a health care system that leads in innovation, delivers affordable, high-quality medicines, and results in healthier people. Thank you for your concern and ongoing leadership as we work on our broader efforts to ensure patients have timely access to innovative, quality, and affordable medications.

If you have additional questions or concerns, please contact Jim Esquea, Assistant Secretary for Legislation at (202) 690-7627. I have sent this response to the co-signers of your letter.

Sincerely,

A handwritten signature in dark ink, appearing to read "SMB", is written over the typed name.

Sylvia M. Burwell

From: Jorgenson, Lyric (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=JORGENSENLA]
Sent: 6/14/2017 8:27:32 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Wolinetz, Carrie (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Wolinetzcdc9a]
Subject: FW: Controversy surrounding ZIKA vaccine development
Attachments: ATT00002.htm; img-511164612-0001.pdf; ATT00001.htm; msf_comments_to_fr_notice_re_zika_vaccine_candidate_licensing.pdf

FYI, adding to the earlier email thread

From: Eiss, Robert (NIH/FIC) [E]
Sent: Wednesday, June 14, 2017 4:26 PM
To: Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>
Subject: RE: Controversy surrounding ZIKA vaccine development

Sanofi [REDACTED] So I
imagine [REDACTED]
[REDACTED]

From: Jorgenson, Lyric (NIH/OD) [E]
Sent: Wednesday, June 14, 2017 4:15 PM
To: Eiss, Robert (NIH/FIC) [E] <eissr@mail.nih.gov>
Subject: RE: Controversy surrounding ZIKA vaccine development

Thanks so much – would you mind forwarding the MSF & governor letters the email refers to?

From: Eiss, Robert (NIH/FIC) [E]
Sent: Wednesday, June 14, 2017 4:11 PM
To: Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>
Subject: FW: Controversy surrounding ZIKA vaccine development

FYI -

This issue was triggered by MSF I think [REDACTED]
[REDACTED]

From: "Lubinski, Christine" <clubinski@idsociety.org>
To: "Global Health Committee" <GlobalHealthCommittee@idsociety.org>
Cc: "Aziz, Rabita" <raziz@idsociety.org>, "McGoodwin, Colin" <CMcGoodwin@idsociety.org>
Subject: Controversy surrounding ZIKA vaccine development

Hello all- Colleagues from the Walter Reed Army Institute for Research reached out to IDSA staff about their concerns about congressional and media attention focused on a potential exclusive license to be granted to Sanofi for one of many Zika vaccine candidates still under development. It appears that widespread concern about drug pricing is spilling over into the vaccine arena and there seems to be little understanding of the vaccine development process not to mention premature pressure to price a vaccine still under development. Colleagues at WRAIR are concerned about the chilling effect this may have on actually getting an efficacious vaccine licensed. I am attaching a letter from MSF and from the governor of Louisiana as well as a couple of press stories about this.

REL0000024383

We just wanted to alert this Committee and the Public Health Committee to this issue, since IDSA may be called upon to comment at some point.

<https://www.statnews.com/pharmalot/2017/05/17/sanofi-us-army-zika-vaccine/>

http://www.huffingtonpost.com/entry/zika-vaccine-sanofi_us_59373298e4b0ce1e7408b9ca?utm_hp_ref=zika

Comments are welcome. Christine

Office of the Governor
State of Louisiana

JOHN BEL EDWARDS
GOVERNOR



P.O. Box 94004
BATON ROUGE, LOUISIANA 70804-9004
(225) 342-7015
GOV.LA.GOV

May 10, 2017

Robert M. Speer
Acting Secretary of the Army
101 Army Pentagon
Washington, DC 20310-0101

Dear Mr. Speer,

As Governor of the State of Louisiana, I write to express my serious concern about the Department of Defense's proposed exclusive license of patents on a Zika vaccine to Sanofi, particularly if the license does not address the pricing of the vaccine to U.S. residents.

Louisiana remains one of the Gulf states most likely to be affected in the event that the Zika virus continues to spread. A decision to give one company, Sanofi, a monopoly, without any constraints on the price for the vaccine, could cripple state budgets and threaten public health in the event of local Zika transmission. As many as 540,000 Louisiana residents on Medicaid alone could benefit from an effective Zika vaccine, but all my constituents deserve access in the event of local transmission. I am concerned that an unaffordable Zika vaccine will unnecessarily expose our state's most vulnerable citizens, our babies, to risk for serious lifelong complications of preventable Zika infection.

It is my understanding that considerable federal support has gone into creating the vaccine, including federally-funded clinical trials, a \$43 million BARDA grant to Sanofi for Phase II trials, with the option for an additional \$130 million in funding for the later trials if needed for the vaccine's approval by the FDA. Sanofi would also be eligible for a valuable priority review voucher, worth millions of dollars, and possibly benefit from several years of exclusive rights on the data from the clinical trials the U.S. government has funded. The extent of public investment in the development of the vaccine calls into question the need for an exclusive license, and it certainly provides a compelling reason to ask questions about the price of the vaccine now, before a license is signed, rather than after a monopoly has been granted.

Furthermore, because the vaccine in question is the Zika Purified Inactivated Virus (ZPIV) and makes use of the inactivated virus to produce an immune response, it may have added benefits and value as a booster vaccination to DNA Zika vaccines. Preliminary studies by NIAID found that the ZPIV induced antibodies that neutralized the virus and protected animals from disease when they were challenged with Zika.

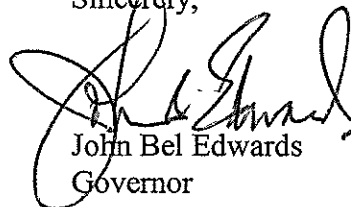
Robert M. Speer
May 10, 2017
Page 2

I am concerned that the Department of Defense has yet to address concerns about pricing and affordability for the vaccine, despite requests from nearly a dozen non-governmental organizations representing patient interests. In April 2017 the Department of Justice ordered Sanofi to repay nearly \$20 million in overcharges to the Department of Veterans Affairs. Sanofi is known to charge U.S. residents far more than residents of other industrialized countries for other medications, such as Sanofi's multiple sclerosis drug Aubagio (teriflunomide).

We believe our interests would be better served by avoiding the grant of an exclusive license on the Army's Zika patents. Barring that, U.S. residents, particularly those that I represent in Louisiana, deserve assurances that the vaccine will be affordable to people who have already paid for most of the research and development costs.

No one should have to worry about their child being born with microcephaly or other birth defects, and certainly no one should have to face that frightening prospect simply because the vaccine is unaffordable. Louisiana taxpayers have already paid once for this invention, and it is reasonable to expect that the Department of Defense at minimum ensure that our residents pay reasonable prices on the other end.

Sincerely,



John Bel Edwards
Governor

cc: Barry Datlof



333 Seventh Avenue, 2nd Floor
New York, NY 10001-5004

Tel: (212) 679-6800
Fax: (212) 679-7016

Web: www.doctorswithoutborders.org

For more information, contact: Judit Rius, U.S.
manager and legal policy adviser & Jen Reid,
advocacy and research officer at
judit.rius@newyork.msf.org

To:
Commander, U.S. Army Medical Research and Materiel Command
ATTN: Command Judge Advocate, MCMR-JA, 504 Scott Street
Fort Detrick, MD 21702-5012 USA

**Doctors Without Borders/Médecins Sans Frontières (MSF) Comments to the Department of
Defense Notice of Grant Intent to an Exclusive License of U.S. Government-Owned Patents on Zika
Vaccine**

January 23, 2017

Doctors Without Borders/Médecins Sans Frontières (MSF) provides the following comments regarding the Notice from the Department of the Army of the United States Department of Defense *of its intent to grant an exclusive, royalty-bearing, revocable license to pending United States Provisional Patent Application 62/ 343,315, entitled, “Zika Virus Vaccine and Methods of Production” filed May 31, 2016 and an exclusive, royalty-bearing, revocable license to pending United States Provisional Patent Application 62/370,260, entitled, “Zika Vaccine and Methods of Preparation” filed August 3, 2016 to Sanofi Pasteur.* Notice appeared in 81 FR 89087 on Friday, December 9, 2016.

MSF objects to the grant of an exclusive patent license and urges the United States government to consider the negative impact an exclusive agreement will have on the development, affordability and availability of a Zika vaccine, which is urgently needed for people affected by the Zika virus in the United States and worldwide. We ask the U.S. government to consider instead granting an open non-exclusive patent license with appropriate and publicly available terms and conditions to help ensure that further development of this U.S. government funded-technology will prioritize all health needs and ensure sustainable and affordable access of any resulting vaccine.

Overview

MSF is an international medical humanitarian organization working in nearly 70 countries. Every year, MSF vaccinates tens of thousands of children, delivering more than 3.9 million doses of vaccines and immunological products in 2014 alone. We need biomedical innovations that improve medical outcomes and are accessible and affordable, including for prevention and treatment of global health emergencies. We hope to use an effective Zika vaccine in our medical operations in the future. MSF, Ministries of Health and people around the world will only be able to benefit from the U.S. government investment if the resulting vaccine is effective, safe, available, affordable and suitably adapted to the resource-limited settings where most people affected by Zika virus live. Through our work, MSF witnesses the everyday impact of having limited or no access to medicines, diagnostics and vaccines, due to the lack of innovation on essential, suitably adapted and affordable medical tools in the contexts and populations where they are most needed.

We recognize the need to reward innovation and finance research and development (R&D). We thank the U.S. government for its funding and leadership in Zika vaccine research. The acceleration¹ of research on Zika vaccine candidates almost a year after the World Health Organization declared the epidemic a global health emergency is very welcomed.

However, an exclusive license to a single pharmaceutical company is unnecessary to promote innovation and instead has the potential of hindering innovation as well as future access to this promising vaccine candidate. The need for an open public health-driven innovation approach is even more important given that this medical technology has been fully funded and is owned by the United States government. The licensing of this technology should ensure full public return on the public investment that U.S. taxpayers have made and are continuing to make.

A vaccine that is not appropriately developed or a vaccine without appropriate measures to ensure access is insufficient and would be a missed opportunity to make maximal use of limited US government resources. The next step in the Zika vaccine development process, including its licensing and technology transfer strategy, needs to ensure that U.S. government funding and leadership in vaccine R&D results in a vaccine that is effective and accessible for all patients in need in the U.S. and globally, including the most neglected. As the latest Ebola outbreak in West Africa should constantly remind us, diseases have no borders in a globalized world. Without a global research and access strategy for the Zika vaccine, Zika will not be fully stopped.

Exclusive patent licensing is not a necessary or appropriate strategy to further develop this Zika vaccine candidate.

MSF objects to the granting of this exclusive license for development of Zika vaccine candidates for the following reasons:

1. The grant of exclusivity is not a reasonable and necessary incentive to promote innovation and further development of a Zika vaccine.

We agree with comments submitted by Knowledge Ecology International and others² that argue that the Army proposal to grant an exclusive license to patents on a Zika vaccine to Sanofi Pasteur (Sanofi) is contrary to the provisions of 35 U.S.C. 209(a)(1). According to U.S. law, the United States government may grant an exclusive or partially exclusive license “only if” the exclusivity is “a reasonable and necessary incentive to call forth the investment capital needed to bring the invention to practical application; or otherwise promote the inventions utilization by the public.” In other words, the U.S. government cannot grant exclusive licenses in cases where the exclusive rights are not reasonable and necessary for the practical application and utilization of the invention.

Before an exclusive license is granted, Sanofi or any other potential recipient of an exclusive license and the U.S. Army have the burden of proving that these exclusive rights are necessary. Pharmaceutical companies usually argue that exclusivity is necessary to recoup investments and risk associated with the research and development process, as well the opportunity cost to work on a given technology, but we argue that this exclusivity is unnecessary to promote innovation and the further development of the vaccine candidate given:

- a. The significant funding and resources that the U.S. government has already dedicated to this vaccine candidate, including more than \$40 million in BARDA grant funding to Sanofi.³

- b. Sanofi and any other vaccine developer that further develops this vaccine candidate are also eligible to receive additional funding, incentives and subsidies from the U.S. government, including the likely lucrative Food and Drug Administration (FDA) Priority Review Voucher (PRV) for neglected diseases, without any product access conditions attached, if a vaccine is successfully registered with the FDA⁴, as well as potentially the different tax credits and exclusivities attached to an orphan drug designation. The FDA voucher itself has been valued on the open market at at least 350 million USD through recent reported transactions.
- c. Sanofi and other vaccine developers may also receive other resources provided by other countries. For example, the funds and resources that will be made available to accelerate vaccine development for emerging infectious diseases with the recently launched Coalition for Epidemic Preparedness Innovations (CEPI) that multiple governments, philanthropies like the Bill & Melinda Gates Foundation and the Wellcome Trust, and MSF are members of.
- d. There is no publicly available information on the investment that Sanofi has made or will need to make to complete development of this vaccine. The financial risk and investment that Sanofi will need to make is limited and predictable, but the potential profitability is considerable. There is an expected profitable commercial market for this vaccine that will provide appropriate incentives for recovering any potential additional investment that Sanofi or any other vaccine developers may need to make to further develop this technology.

2. The grant of patent exclusivity can hinder innovation for Zika vaccines and doesn't allow research strategies that promote collaboration and focus on neglected medical needs.

The grant of exclusive rights in the US government-owned patents is not the best tool to promote innovation and can hinder innovative efforts on Zika vaccine development. Even where government funding does lead to important advances in biomedical innovation, these investments still do not necessarily lead to effective prioritization of further R&D and successful outcomes driven by patients and public health needs if the appropriate licensing and technology strategy is not pursued.

- a. An exclusive license will give Sanofi a monopoly in the research, manufacturing and sale of the technology and will allow Sanofi to exclude competition in the clinical development as well as in the manufacturing and pricing of this technology.
- b. The grant of exclusivity does not ensure that the Zika vaccine development process will target the populations most in need. Sanofi will be allowed to pursue research strategies to maximize use of the vaccine candidate in profitable markets, like the U.S. or the travel market, limiting or excluding clinical development of competing research agendas that should include a broader and diverse geographical scope to ensure any resulting vaccine is effective and useful in the full range of populations who may need this vaccine, including neglected patients in Africa and other neglected regions.⁵
- c. The grant of exclusivity does not ensure that a vaccine will be developed or that it will adhere to a timely development process. The recent announcement on promising results of clinical trials of rVSV Ebola vaccine that MSF supported shows the importance of government funding and leadership for vaccine development. It also shows how the Canadian government's exclusive licensing was unnecessary and tragically delayed urgently needed innovation. It was thanks to initial studies at a Canadian government laboratory that the VSV-EBOV vaccine was confirmed as potentially effective against Ebola. Despite the fact that the government licensed this vaccine to a U.S. company, NewLink, four years before the West African Ebola outbreak, the project stalled and the vaccine was not made available to people at risk for more than five years. If at least Phase

If clinical trials had been conducted prior to the most recent outbreak, the vaccine could have been deployed during the emergency and potentially helped save lives. This wasted opportunity and failure to advance the vaccine's development nevertheless netted NewLink more than \$63.5M profit when they sold the rights to pharmaceutical company Merck during the most critical phase of the outbreak. A non-exclusive license could have allowed the Canadian government, either prior to or during the outbreak, to take more decisive action to encourage or require the timely testing and development of the vaccine.

3. An exclusive license can be a barrier to ensuring a Zika vaccine will be available and affordable to all who need it.

The high price of vaccines is already a key medical and operational challenge for MSF and many governments. By 2014 the price to fully vaccinate a child in the poorest countries of the world was 68 times more expensive⁶ than it was in 2001. The price in other countries is even higher. Many countries, especially countries considered middle-income economies, are often unable to afford new high-priced vaccines that prevent countless deaths from vaccine-preventable diseases such as childhood pneumonia.

Before granting a license on U.S. government-owned rights, the U.S. government should ensure that the license will ensure that the "benefits" of the invention will be "available to the public on reasonable terms," a requirement of 35 U.S.C. §201(f). Granting an exclusive license to a vaccine manufacturer will not only fail to ensure any resulting vaccine is available on reasonable terms, but can also become a significant barrier to the future availability and affordability of the vaccine.

As the vaccine development has been publicly financed by the U.S. government, the price of any resulting vaccine should be closely aligned with production costs. Yet, an exclusive license to Sanofi will allow the company to charge high prices based on what their targeted markets will bear regardless of actual costs. Based on our experience, leaving these decisions exclusively to a pharmaceutical company may not lead to appropriate public health outcomes. We hope Sanofi commits to and implements an appropriate access and manufacturing strategy, but it is relevant for the U.S. government to know that when left to decide strategy without government oversight, Sanofi has failed previously and currently to ensure uninterrupted manufacturing, supply and affordability of essential medical tools for which they are the sole supplier. For example, Sanofi's pricing strategies for its inactivated polio vaccine⁷ and dengue vaccine⁸ are a barrier to access for many middle-income countries.

While MSF continues to be challenged by high prices of medical tools, we know that high prices are avoidable and affordable innovation is possible. In 2001, high prices left MSF limited in our ability to save the lives of people living with HIV. At the time pharmaceutical companies charged MSF, governments and patients an astronomical US \$10,000 per person, per year for antiretroviral medicines used to treat HIV. This meant that MSF and governments, in the face of thousands of people dying daily from AIDS-related illnesses, could only provide treatment to a very limited number of people. In response, affected governments and civil society applied legal safeguards to remove patent barriers and foster generic competition. HIV treatment costs fell, virtually overnight, to one US dollar a day per person.⁹ As a result of competition among generic medicines producers, prices for first-line HIV medicines have continued to fall and today more than 18 million people receive treatment,¹⁰ including through U.S. government-funded programs such as the President's Emergency Plan For AIDS Relief (PEPFAR) and the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund). In 2012, generics accounted for 96 percent of all treatments purchased by donor-funded programs such as the Global Fund.¹¹

An exclusive license will also be barrier to competition in the manufacturing and supply of the technology, as it will allow Sanofi to exclude other manufacturers from producing and selling the technology. Promoting competition is the best tool to ensure affordability as well as ensuring sufficient manufacturing and supply

of any resulting vaccine. MSF and patients have repeatedly experienced the consequences of what happens when a single supplier discontinues manufacturing of an effective and needed product for conditions affecting neglected populations. For example, in 2010, due to limited profitability, Sanofi decided to stop manufacturing an important antivenom to treat deadly snake bites. The company did not reveal this decision until 2013, resulting in a worldwide supply shortage of a critical antivenom before a replacement product can be launched.¹²

A better way to promote U.S. government funded innovation: open non-exclusive licenses with terms and safeguards for patient-driven innovation and future affordable access

An exclusive license fails to address the need for an innovation strategy that put the needs of all patients and vaccine providers at the center of the biomedical innovation system. Instead, MSF recommends that the U.S. government consider an open licensing and technology transfer strategy to allow Sanofi and a variety of vaccine developers and researchers to test and further develop this vaccine, promoting a variety of scientific, research, development, business and delivery approaches. The licensing of this technology should include the creation of terms and conditions that will act as safeguards to ensure that the development will be patient-driven and that any resulting vaccine will be safe, effective, appropriately available and affordable to all people in need. We also recommend that the U.S. government make the terms and conditions of the license publicly available to allow for appropriate review, accountability and implementation of the safeguards created.

Granting an open non-exclusive license with the appropriate terms and conditions will have at least the following positive public health impact:

1. An open license can help promote timely development of the vaccine candidate.

An open, non-exclusive license not only ensures that multiple companies can move towards developing the product, but can ensure that if one company fails to meet milestones or advance development, the patent holder (the US government) can move on to others and not have their hands tied. A non-exclusive license allows several vaccine developers to pursue different research, regulatory and development strategies of the vaccine candidate, and also can reduce the negative health impact of research stalled or delayed by a single researcher strategy. For example, in the case of the rVSV Ebola vaccine highlighted above, had the Canadian government granted an open license, governments and medical service providers such as MSF would not have been dependent on the development timeline of only one company.

2. An open license will allow interested companies to test the safety and efficacy of the vaccine candidate in a variety of populations and contexts.

An open license allows several companies and vaccine researchers to test the effectiveness and safety of the technology in a variety of settings, including pursuing research strategies that target the needs of neglected populations due to expectation of limited profitability and/or knowledge gaps on Zika epidemiology in Africa.

3. An open license will help ensure stable supply.

An open license allows several companies to manufacture a resulting vaccine and reduces the public health liability created by a single manufacturer that decides to stop manufacturing or is not able to meet the global demand of a successfully developed Zika vaccine.

4. An open license will help ensure affordable access.

An open license may facilitate the emergence of competition in the manufacturing and supply of Zika vaccines, which is ultimately the best tool to promote affordability.

U.S. government can lead the way on creating new models for research and development for essential medical tools

The reliance on the creation and granting of exclusivities to pharmaceutical companies in R&D of essential medical technologies is a flawed paradigm for funding and promoting innovation. This often leads to limited access while failing to stimulate open and patient-driven innovation. It is even less rational when the United States is already funding and de-risking the development of the medical technology as is the case with the Zika vaccine.

New approaches are needed not only to avoid US taxpayers paying twice¹³ – first by paying a significant percentage of the R&D costs and second by paying high prices – but also to ensure that the vaccine development and manufacturing process will be public health-driven and benefit all in need, especially for essential medical tools like vaccines needed for emergencies and epidemics.

MSF has for years raised the alarm about the challenges of high prices and need for new incentives to promote innovation that do not rely on monopolies and exclusivities. In our experience, both as a medical provider and funder of innovation,¹⁴ competition and open access to essential medical technologies is a useful tool to reduce prices and promote supply security and therefore increase access to resulting technologies. MSF recently published a report on biomedical innovation, “Lives on the Edge: Time to align medical research and development with people’s health needs,”¹⁵ that provides an overview of some the challenges with the current innovation system and our proposals on steps governments need to take to improve it.

New approaches to promote medical innovation, including approaches that MSF and others have supported, are demonstrating that affordable and accessible medical breakthroughs are possible. This is particularly true when intellectual property is openly pooled, like with the UNITAID-Medicines Patent Pool – which the US National Institutes of Health was the first to join, to promote competition in the HIV/AIDS drug development¹⁶ – and when incentives break the link between the cost of R&D and the price and sale of the end product.

There are ongoing efforts in international fora to consider how this could be achieved, including in the commitments made by the United States and other governments on new models for biomedical innovation that de-link R&D costs from prices in recent years at the World Health Assembly following the Report of the Consultative Expert Working Group on R&D Financing and Development (CEWG report) and most recently through the 2016 UN Political Declaration on Antimicrobial Resistance. In the same direction, the recently released report of the UN Secretary General’s High Level Panel on Access to Medicines made a variety of recommendations,¹⁷ including increasing transparency and reforming incentives for innovation, especially for the licensing of publicly funded research.

Conclusion

At a time when the high price of life-saving medical tools, including hepatitis drugs, biologics and vaccines, is becoming a barrier to effective medical care worldwide and medicines are being rationed because of high prices in the U.S. and around the world, it is very concerning to see the U.S. government considering locking in a development deal that will limit innovation and will not safeguard affordable access to the resulting

vaccine. Instead of creating new exclusivities for pharmaceutical companies by giving away exclusive rights on publicly funded innovation, the U.S. government should pursue R&D strategies that promote open and collaborative innovation and ensure affordable access to resulting products.

¹ Thomas K. The Race for a Zika Vaccine. New York Times. 19 November 2016. Available from: <https://www.nytimes.com/2016/11/20/business/testing-the-limits-of-biotech-in-the-race-for-a-zika-vaccine.html> and, Pellerin C. Human Trials Begin for Army-Developed Zika Vaccine. US Department of Defense. 8 November 2016. Available from: <https://www.defense.gov/News/Article/Article/999584/human-trials-begin-for-army-developed-zika-vaccine>

² Comments by KEI and others. An exclusive license to patents on a new Zika vaccine to Sanofi is contrary to the provisions of 35 U.S.C. 209(a)(1). Submitted 12 January 2017. Available from: <http://keionline.org/sites/default/files/Zika-12Jan2016-KEI-AFSCME-PFAM-UAEM-BAKER-35USC209a1.pdf>

³ Pellerin C. Army Researchers, Sanofi Pasteur to Co-Develop Zika Virus Vaccine. Department of Defense. 7 July 2016. Available from: <https://www.defense.gov/News/Article/Article/830751/army-researchers-sanofi-pasteur-to-co-develop-zika-virus-vaccine>, and Sagonowsky E. Sanofi grabs \$43M in U.S. government funds to advance Zika vaccine into Phase I. FiercePharma. 26 September 2016. Available from: <http://www.fiercepharma.com/vaccines/sanofi-grabs-43m-u-s-government-funds-for-zika-vaccine-r-d>

⁴ Brock W, Cohen R, Cone J, McKenna L. The Zika loopholes. Politico. 25 March 2016. Available from: <http://www.politico.com/agenda/story/2016/03/the-right-way-to-encourage-companies-to-develop-a-treatment-for-zika-000079>

⁵ Adams P, Nutt C. A Zika Vaccine, but for Whom? New York Times. 28 December 2016. Available from: https://www.nytimes.com/2016/12/28/opinion/a-zika-vaccine-but-for-whom.html?_r=0

⁶ MSF. The Right Shot: Bringing down barriers to affordable and adapted vaccines, 2nd ed. January 2015. Available from: <https://www.msfaccess.org/our-work/vaccines/article/2345>

⁷ MSF. MSF responds to inactivated polio vaccine price announcement. 4 March 2014. Available from: <https://www.msfaccess.org/content/msf-responds-inactivated-polio-vaccine-price-announcement>

⁸ Coconuts Manila. DOH: We can't afford to give free dengue vaccine to everyone. 22 February 2016. Available from: <http://manila.coconuts.co/2016/02/22/doh-we-cant-afford-give-free-dengue-vaccine-everyone>

⁹ Médecins Sans Frontières. Untangling the Web of Antiretroviral Price Reductions, 17th edition. July 2014. Available from: http://www.msfaccess.org/sites/default/files/MSF_UTW_17th_Edition_4_b.pdf

¹⁰ UNAIDS. Fact sheet November 2016. Available from: <http://www.unaids.org/en/resources/fact-sheet>

¹¹ UNITAID. HIV Medicines Technology and Market Landscape. March 2014. Available from: <http://www.unitaid.eu/images/marketdynamics/publications/HIV-Meds-Landscape-March2014.pdf>

¹² MSF. Snakebite: How Sanofi slithered its way out of the neglected antivenom market. July 2015. Available from: https://www.msfaccess.org/sites/default/files/NTDs_Brief_FavAfrique_ENG_2015.pdf

¹³ An exclusive license will undermine existing United States domestic and global commitments towards the fight against Zika. The Congressionally approved Zika funding totals at least \$1.1 billion in 2016. Source: The Status of Funding for Zika: The President's Request, Congressional Proposals, & Final Funding - <http://kff.org/global-health-policy/issue-brief/the-status-of-funding-for-zika-the-presidents-request-congressional-proposals-final-funding/>

¹⁴ See for example, http://www.dndi.org/wp-content/uploads/2009/03/DNDi_Modelpaper_2013.pdf and MSF's proposal for a better model for TB R&D regime development: <http://www.msfaccess.org/spotlight-on/3p-project-new-approach-developing-better-treatments-tb>

¹⁵ MSF. Lives on the Edge: Time to align medical research and development with people's health needs. May 2016. Available from: <http://www.msfaccess.org/content/report-lives-edge-time-align-medical-research-and-development-people%E2%80%99s-health-needs>

¹⁶ Chen H. US Government First to Share Patents with Medicines Patent Pool. The White House. 30 September 2010. Available from: <https://www.whitehouse.gov/blog/2010/09/30/us-government-first-share-patents-with-medicines-patent-pool>

¹⁷ Full report and submissions to the UN Secretary General High Level Panel on Access to Medicines, available from: <http://www.unsgaccessmeds.org/>

From: Petrik, Amy (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=C4EC05A179F04067B61F20605E911E7C-PETRIKA]
Sent: 11/7/2017 6:52:54 PM
To: Mowatt, Michael (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb1ef7e2e54b4164ae34814574bda638-mmowatt]; Feliccia, Vincent (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7f3a54860cb941c1abe1df786e478e00-vfeliccia]; Salata, Carol (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f98ca6a1f9fc4cfdbbf4036ca8cbace4-csalata]; Green, Wade (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=88fdd3b0456c40458e952e6c043b2a6b-williamswa]; Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Stover, Kathy (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c82722674ba14c2f969bd50dfa6a7af4-stoverk]
Subject: FW: Web Inquiry regarding: (E-181-2016/0)

Hi Everyone,

Just FYI -- a new inquiry from KEI below.

Thanks,
Amy

From: James Love [mailto:james.love@keionline.org]
Sent: Tuesday, November 07, 2017 1:39 PM
To: Petrik, Amy (NIH/NIAID) [E] <amy.petrik@nih.gov>
Subject: Re: Web Inquiry regarding: (E-181-2016/0)

For example, is the license to PaxVax directed at this vaccine?

VRC 320: A Phase I, Randomized Clinical Trial to Evaluate the Safety and Immunogenicity of a Zika Virus DNA Vaccine, VRC-ZKADNA090-00-VP, Administered Via Needle and Syringe or Needle-free Injector, PharmaJet, in Healthy Adults

On Tue, Nov 7, 2017 at 1:25 PM, James Love <james.love@keionline.org> wrote:

Amy, what the status of clinical testing of the vaccine you are licensing?

Jamie

--

James Love, Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: [+1.202.332.2670](tel:+12023322670), US Mobile: [+1.202.361.3040](tel:+12023613040), Geneva Mobile: [+41.76.413.6584](tel:+41764136584), twitter.com/jamie_love

--

James Love. Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

From: Joe Allen [jallen@allen-assoc.com]
Sent: 12/7/2017 4:06:55 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]
Subject: Re: KEI Op-ed in the Hill urging HHS nominee Azar to march in to control drug prices

I'm emailing with Jessica Seebok and Michael Waring on who can best reply. They suggested a patient's advocacy group or BIO. I offered to if neither is interested. If you have other thoughts, let me know and we'll throw it into the mix.

On 12/7/2017 11:02 AM, Rohrbaugh, Mark (NIH/OD) [E] wrote:

> Are there legal academics who will publish their views, even in an op ed, on the statutory basis for march-in?

>

> -----Original Message-----

> From: Joe Allen [mailto:jallen@allen-assoc.com]

> Sent: Thursday, December 07, 2017 10:03 AM

> To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>

> Subject: KEI Op-ed in the Hill urging HHS nominee Azar to march in to control drug prices

>

> They never quit. Here's their latest:

> <http://thehill.com/opinion/healthcare/363322-american-taxpayers-will-be-alex-azars-shareholders-lets-hope-he-can-serve>

>

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

REL0000024385

From: Hardesty, Rebecca (NIH/OD) [C] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=21465CEB763947408D209AAABF10AF70-HARDESTYRS]
Sent: 10/15/2018 6:08:08 PM
To: Fennington, Kelly (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3e2d306aa244429b0f51d365bd24a26-fenningk]; Bruff, Susan (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d3bdf8cac94049dcab28d2eb5fad5137-bruffs]; Jorgenson, Lyric (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3bbde7d361374981a4d336b6eeb17521-jorgensonla]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Bayha, Ryan (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5d5a4353cd514322a8598dbb1751ee79-bayhar]; Tucker, Jessica (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2baf4ae78d90412dbefbfb5e52c31a4-tuckerjm]; Bonham, Valerie (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dd4040eaa26541a8b30fc274e52aba59-bonhamva]; Kukic, Ira (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=df851c54f7714bc6a88567ccfa9cf62b-kukici2]; Baden, Elizabeth (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8b3ba758e2944c50b85eb427839e4716-badenem]; Berger, Adam (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cfbf537ab62640ffa150a8f65241879f-bergerac]
CC: Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaaf06ebd70-parkeras]; Ampey, Bryan (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9672b522d0b34f3792e2934dac636a57-ampeybc]

Subject: Weekly OSP Senior Leadership Meeting

Attachments: OSP Senior Staff Meeting 101618.docx

Location: 1/103 | Dial: b6

Start: 10/16/2018 4:00:00 PM

End: 10/16/2018 5:00:00 PM

Show Time As: Tentative

Recurrence: Weekly
every Wednesday from 10:00 AM to 11:00 AM

Required Attendees: Fennington, Kelly (NIH/OD) [E]; Bruff, Susan (NIH/OD) [E]; Jorgenson, Lyric (NIH/OD) [E]; Rohrbaugh, Mark (NIH/OD) [E]; Bayha, Ryan (NIH/OD) [E]; Tucker, Jessica (NIH/OD) [E]; Bonham, Valerie (NIH/OD) [E]; Kukic, Ira (NIH/OD) [E]; Baden, Elizabeth (NIH/OD) [E]; Berger, Adam (NIH/OD) [E]

Optional Attendees: Parker, Ashley (NIH/OD) [E]; Ampey, Bryan (NIH/OD) [E]

Updated agenda.



OSP Senior Staff
Meeting 101618....

REL0000024386

OSP Senior Staff Meeting
Tuesday, October 16, 2018
10:00 – 11:00 AM

Agenda

b5

Telecon information:

Dial-in	b6
Leader Code	b6
Participant Code	b6

From: Stevens, Ashley J [astevens@bu.edu]
Sent: 5/22/2019 9:46:47 AM
To: Rohrbach, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: Fwd: Quick Q

Can you get data on the Federal investment in testing Xtandi? I recall one small grant.

Sent from my iPhone -- please excuse typo's

Ashley J Stevens
Focus IP Group LLC
Winchester, MA 01890
USA
Phone: (781) 721-2670
Cell: b6
Email: astevens@bu.edu

Begin forwarded message:

From: Frederick Reinhart <fred@research.umass.edu>
Date: May 21, 2019 at 21:38:28 EDT
To: "Stevens, Ashley J" <astevens@bu.edu>
Subject: Re: Quick Q

Jamie Love suggested in his IP Watchdog article that the feds paid a lot and their total investment Re to Xtandi was over \$1 billion

Fred

Sent from my iPhone

On May 21, 2019, at 8:03 PM, Stevens, Ashley J <astevens@bu.edu> wrote:

Not much.

Sorry this is too late

Sent from my iPhone -- please excuse typo's

Ashley J Stevens
Focus IP Group LLC
Winchester, MA 01890
USA
Phone: (781) 721-2670

Cell: b6

Email: astevens@bu.edu

On May 21, 2019, at 14:48, Frederick Reinhart
<fred@research.umass.edu> wrote:

Ashley, I am getting on a phone call in 10 minutes with Doctors
Without Borders and we are talking about KEI. Do you by chance
know how much federal support was provided for clinical trials on
Xtandi? Fred

Sent from my iPhone

From: Yang, Jasmine (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DCACD5B675E74725A0D6A6FC9A130431-YANGJJ2_6B5]
Sent: 1/11/2019 7:39:42 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]
CC: Rodriguez, Richard (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8092cb5394e04733ac0d4d84d25f65e5-rodrigr]; Thomas, Jeffrey (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f7b9fca6f5634a45ba8802d6f6c8a410-jeffreyt]
Subject: FW: KEI Response to Jasmine's FRN
Attachments: 2019-01-10_LetterToKEI_A-066-2019_2.docx

Hi Dale and Mark,

Thanks for cleaning up the KEI letter.

b5

b5

Let me know if you disagree.

Thanks,
Jasmine

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, January 10, 2019 1:06 PM
To: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Cc: Yang, Jasmine (NIH/NCI) [E] <jasmine.yang@nih.gov>; Thomas, Jeffrey (NIH/NCI) [E] <jeffreyt@mail.nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: RE: KEI Response to Jasmine's FRN

Thanks Richard. Dale and I have reviewed this:

b5

b5

From: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Sent: Thursday, January 10, 2019 9:00 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Yang, Jasmine (NIH/NCI) [E] <jasmine.yang@nih.gov>; Thomas, Jeffrey (NIH/NCI) [E] <jeffreyt@mail.nih.gov>
Subject: KEI Response to Jasmine's FRN

Hi Mark,

We have further adjusted Jasmine's response and believe it is ready to go back to KEI.

b5

b5

b5

b5

Please let us know if you have additional thoughts.

Thanks,

Richard

RICHARD U. RODRIGUEZ
Associate Director
Patent Agent

Technology Transfer Center
National Cancer Institute
National Institutes of Health
9609 Medical Center Drive, Rm 1E530
Bethesda, MD 20892-9702 (for business mail)
Rockville, MD 20850-9702 (for courier service/visitors)
Phone (Main Office): 240-276-5530
Direct phone: 240-276-6661
Fax 240-276-5504
richard.rodriguez@nih.gov
<https://techtransfer.cancer.gov>

"Start by doing what's necessary; then do what's possible; and suddenly you are doing the impossible" - Francis of Assisi

Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, copying or use of this email or the information enclosed therein is strictly prohibited, and you should notify the sender for return of any attached documents.

REL0000024389

b5

b5